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ON THE RELATION OF ANATOMICAL STRUCTURE AND OF ANTAGONISM BETWEEN ORGANS TO DISEASE

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IT is not my intention to deal here with, or enlarge upon, those subjects which have been so admirably and completely presented by Dr. Adami, Dr. Gurd, Dr. Rhea and Dr. Meakins. Indeed, if I arise to speak at all, it is only to add a few remarks on certain phases in the development and course of disease which have for some time past attracted the attention of pathological anatomists and which have perhaps not received that regard which they deserved in the study of infectious diseases.

There are two points which I should like briefly to bring to your attention: first, the relationship of anatomical structure or architecture of an organ to disease, its development and termination; second, the effect of certain, as yet poorly understood, internal antagonistic actions and relations of organs, which, in a manner now well recognized in embryonic development, may play a part in the history of disease and, for that matter, perhaps in the whole life and death of animal organisms.

Let me, in order to make myself clearly understood, illustrate these points by concrete examples.

We know, for instance, that in pneumonia, quite apart from the virulence of the pneumococcus and the general resistance of the individual, the arrangement of lung tissue has much to do with the origin, development and course of this disease. A person with a marked emphysema, acquired or senile, will react quite differently to this infection to one in whom elasticity and structures of lung tissue have been normally preserved. Not only will the emphysematous

Opening the discussion on Immunity at the Medico-Chirurgical Society of Montreal, December 4th, 1914.

person be, for anatomical reasons, more liable to contract pneumonia, but the course and outcome of the disease will be argely determined by the changes in architecture of that organ. For a good termination in pneumonia depends materially on an unhindered removal of inflammatory products through the rich network of lymphatics which are normally carried in the inter-alveolar septa and which receive the softened fibrinous exudate largely through the influence of the elastic tissue carried within the walls of the alveoli; on the other hand, bad terminations such as chronicity, abscess, gangrene, even death are apt to follow when the elasticity and those resorbing surfaces which are essential to the removal of inflammatory products have been lost, or greatly reduced by emphysema or by old age.

In other words, quite irrespective of the character of an infection and the ability of the organism to combat it, certain coarser, if you like, anatomical factors are important in determining the origin and history of the disease. I have, for the sake of brevity, chosen this simple and plain example, but others and more complicated ones in practically all organs of the body could be added to illustrate that the architecture of an organ is of prime importance in any disease which may attack it and that we must consider this as well as the more general features of infection and cell reaction.

The second point to which I would like to draw your attention is, perhaps, more difficult to make plain on short notice and in the few words at my disposal to-night. It rests upon certain embryological observations to which pathologists have given little attention in the past, but which deserve, I believe, careful consideration and study in the future.

My own interest was directed to it some time ago while investigating the development of the normal human kidney, and I shall use this as an example, because it illustrates what I propose to bring before you perhaps better than other similar embryological phenomena.

The kidney develops, as is well known, by a series of three more or less distinct organs: pronephros, mesonephros, and finally, metanephros or permanent kidney. The kidney discloses in this manner phylogenetic evolution plainer than other organs. Now it is interesting and instructive to note that, as each succeeding kidney makes its appearance in the embryo, its predecessor degenerates, wastes and is lost. The phenomena leading to this loss are particularly well exhibited by the mesonephros, which presents a much higher stage of evolution than the pronephros, possessing well developed glomeruli and tubules, really being only an abbreviated metanephros or permanent kidney. Even the mesonephros degen-

erates early in embryonic life with the exception of certain glandular middle parts which enter into the service of the sex glands, where they become, in the female, only accessory parts (paroöphoron, duct of Gärtner and parovarium), in the male, functionating sexual structures (vasa efferentia, coni vasculosi, paradidymis, vas deferens, ejaculatory duct, seminal vesicles). No parts enter into the formation of the permanent kidney.

Now, how is this loss of mesonephros accomplished?

If we investigate this during the various stages of its destruction, we observe changes which are very similar to a severe exudative and productive nephritis. Destruction of Malpighian corpuscles occurs by an engorgement of capillary loops, hæmorrhagic extravasation into capsule, sometimes sufficient to destroy the whole tuft, fusion of capillary loops with adhesions to capsule, and, finally, overgrowth by small round cells which at first form periglomerular infiltrations. At the same time the epithelial cells of the convoluted tubules undergo marked and various forms of parenchymatous degeneration with nuclear kariolysis, desquamation, cast formation and proliferation. Cell infiltration and thickening of the intertubular septa becomes marked and finally the tubules are overgrown by small round cells which later enlarge and assume the characters of distinct spindle cells. In other, notably the posterior, parts of the mesonephros, pure degenerative changes seem to predominate, while later the middle preserved part is gradually drawn by cicatricial tissue to the side of the sex gland into which it is incorporated.

In other words, the loss of the mesonephros, which is a perfectly normal physiological process of development, presents features which are so close to what we observe during post-natal life under pathological conditions in the inflammations of the kidney that we properly term it an acute destructive mesonephritis. Now, that is the remarkable part of it. We have before us a normal inflammation, so to speak, which cannot be traced to bacterial or other foreign toxic action at all; its cause must lie within physiological actions and processes of development; it must be due to agencies within the organism, an auto-intoxication, if that term is here permissible, of the developing embryo.

What are its causes?

It would lead me here too far to go into a detailed discussion of this matter and I refer those who are more especially interested to a full consideration of this question in an article on the physiological degeneration of the mesonephros, published by me in the *Archives of Internal Medicine*, vol. xiii, p. 170, May, 1914.

It must suffice here to state that such phenomena in the embryo (there are many others, as, for instance, the disappearance of the thymus) must be attributed, in all probability, to antagonism of organs. Thus, in the destruction of the mesonephros, we are able to trace it directly to the adjoining sex gland, which ultimately consumes its remains. As the organism presents remarkable examples of altruism with which we are familiar in the action of hormones, so it exhibits and depends for its life, development and maintenance, much like any other state of individuals, upon tissue and organ antagonism, and this force appears, like many others, plainest and accentuated in the developing embryo. These considerations have, to a certain extent, at least, been emphasized by Boll and Roux. But we may go further in view of this close similarity between embryological and pathological processes here described and ask more specifically whether similar phenomena continue after birth? In other words, if, as seems highly probably, antagonism of organic units is one of the moving forces in the life of all individuals, from practically the first division of the ovum to death, may it not enter more than hitherto supposed into production, manifestation and outcome of diseases? Perhaps etiology has, for practical reasons, been too anxious to attach an almost exclusive importance to external causes of disease and has neglected a study of those internal conditions which prepare and make possible the development and specificity and, possibly, also the termination of morbid processes.

How much infections, specificity of diseases and reactions of the organism to infections depend upon infective agents and how much upon the soil and proper balance of the various components of the soil are problems which to-day are not as easily disposed of as was thought in the early days of bacteriological research. The most recent tendency in our ideas is, again, it seems to me, towards a greater rôle of the soil, and this latter has also acquired greater importance in view of the recently revived ideas about the transmutation of bacteria, and their specificity; and in regard to the action on tissues of well-known bacilli, like the tubercle bacillus.

Similar problems and questions arise in the subject under discussion to-night, particularly when we come to the complicated question of treatment by sera or vaccines.

We must, in order to arrive at a satisfactory knowledge and understanding of pathological processes and their intelligent treatment, concentrate all available rays of light upon them and avoid the danger of any one-sided investigation and interpretation of the problems of infection and immunity.

PARENTERAL DIGESTION AND IMMUNITY

By J. George Adami, M.D., F.R.S.

ASKED to introduce this evening's discussion upon immunity, it would, I think, be most serviceable if I placed before you in outline the more recent developments in our views regarding the essential nature of the processes which lead up to the production of the immune state.

All here present will have, I doubt not, a vivid memory of the earlier phases through which we have passed. The first phase was the empirical and lasted up to the recognition of the existence of pathogenic microbes: during this it was admitted that one attack of many infections was followed by resistance to subsequent attacks and there stood out the one solitary application, namely, Jennerian vaccination. The second phase, in the eighties and early nineties, was one of confusion, when, recognizing that the infections were of microbic causation, and being successful in isolating the causative agents, we found that each different pathogenic agent had a distinct *modus operandi*. On the one hand it was found that organisms like the diphtheria bacillus and tetanus bacillus in their growth outside the body produced diffusible toxins, and Behring, Roux and others discovered that the immunity which developed was antitoxic, and on the other hand the majority of pathogenic microbes were found to produce no noticeable ectotoxins, and such immunity as was obtainable was not antitoxic but bactericidal, the fluids of the immunized animal bringing about the solution and death of the causative bacteria.

Rapidly following upon this came the discovery in France and Germany by Bordet and Pfeiffer, respectively, that the latter form of immunity demanded the presence of two orders of substances in the body fluids of the immunized animal. How great was the confusion is indicated by the fact that for one of these, Pfeiffer's "immune body" and Bordet's "*substance sensibilatrice*", the other names of "amboceptor", "*fixateur*", "intermediate body", "sensitizer", "preparator", "desmon", "copula", were proposed by

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* Contributed to the discussion upon recent advances in the theory and practice of Immunity, held at a meeting of the Montreal Medico-Chirurgical Society, December 4th, 1914.

various workers. Nor was the confusion lessened by the continuing fight between the German *humoralists* who were satisfied to study the phenomena manifested by the body fluids alone, and the Franco-Russian *cellularists*, led by Metchnikoff, who, with broader histological insight, laid stress upon the cellular reactions to infection.

The third phase was that of the ascendency of Ehrlich's "side-chain theory" of immunity. It was found that antibodies present in the blood serum neutralised the toxins; all the indications were that chemical interaction went on between the two, but toxins were active in such extraordinary minute quantities, and also were produced in such minute quantities that chemical methods of analysis revealed nothing beyond the probability that they were to be regarded as protein degradation products. The biological test was far more delicate than the chemical. We were, in fact, beyond the realms of chemical technique. If confusion were not to be worse confounded, it was necessary to have some working plan whereby to visualize the processes that went on in the reaction between the microörganism and its products, and the organism. This Ehrlich afforded in his celebrated side-chain theory. Some may to-day criticize that theory, and may gird at its toxins, toxoids and toxones, its haptophores of the first, second and third orders, its end-piece and mid-piece of the complement, but unquestionably it afforded a working scheme, whereby a common basis for expression of phenomena was afforded, and equally unquestionably it promoted an enormous burst of activity in the study of immunity problems. What is more, although Ehrlich cautiously refrained from suggesting or promising any particular element in the cell as being provided with side-chains, his theory was based upon the only rational conception of cell metabolism—that which regards the molecule of living matter as of extraordinary complexity, and in a state of constant unsatisfaction, built up by linking on other simple molecules, and as constantly, in the performance of function, giving up or discharging into the surrounding medium these and other molecular complexes which it has elaborated.

In my "Principles of Pathology" published in 1908, I called attention to certain defects in Ehrlich's theory, and pointed out how it might be brought into fuller conformity with actual knowledge of general cell activities and of enzyme action. I laid down that throughout the whole study of immunity we deal with "the methods by which living matter, whether animal or vegetable, reacts towards other living matter, whether animal or vegetable, and the products

of the same which come in contact with it, and although," I continued, "the statement may at first encounter appear to be both novel and extreme, further thought will confirm it; the problems of immunity narrow themselves down to special problems bearing upon the assimilation and digestion of unusual proteid matter." I might have added, for my treatment of the subject was consistently along these lines, that they resolve themselves into studies of enzyme action.

Long years ago, in the early eighties, I remember Sir Michael Foster teaching us that the assimilation of foodstuffs evidently demanded that more complex molecules of foodstuffs were not built into the cell direct, but were first broken down into their simpler constituent molecules, and of these the molecules common to the constitution of the foreign foodstuffs and to the cells are taken up by the latter, and used for building-up purposes. This view to-day is universally accepted, more particularly as the result of Emil Fischer's studies upon the chemical constitution of proteins, and demonstration that these are complexes formed by the union of varying proportions of mono- and diamino-acids. The Germans speak of this as the 'Baustein,' or building-stone theory. It is a familiar fact that proteids taken as food, while they disappear from the intestinal contents, are not to be detected in the blood and lymph coming from the intestinal tract. And this is true not only of the fully-formed proteins, but also of the peptones and proteoses of the alimentary canal resulting from the disintegration of the larger protein molecules into simpler soluble proteins of the second order. Indeed we have this remarkable fact that if, instead of allowing them to be absorbed and acted upon by the intestinal mucosa, we introduce these peptones and proteoses directly into the circulation, they are found to be highly toxic. There is evidently, therefore, a pronounced difference between *enteral* or intestinal, and *parenteral* digestion, the breaking down, that is, of foreign proteins introduced into the organisms outside of, and without the intermediation of, the digestive tube.

We owe to Victor Vaughan, of Ann Arbor, and his long continued studies from 1901 onwards, the demonstration of the fact that outside the body, by the simple procedure of digestion with several times its bulk of absolute alcohol in the presence of 2 per cent. of sodium hydroxide, any protein, even so apparently harmless a body as egg albumen—is split up into a poisonous and a non-poisonous moiety, the former soluble in alcohol, the latter insoluble, and this poisonous moiety, when introduced into the system other

than through the intestine, is rapidly fatal in doses so minute as from 8 to 100 mg. per guinea-pig. Evidently in the process of passage through the intestinal mucosa, either this poisonous moiety of the protein molecule is detoxicated, or protein disintegration there is so carried on that it is never given off.

The high significance of these observations lies in this, that the bacterial bodies are largely compounded of proteins, that bacterial bodies similarly treated give these same poisonous and non-poisonous moieties: that the process of destruction of bacteria that have gained entrance into the tissues is one of parenteral digestion, and that the phenomena associated with parenteral digestion must therefore be closely studied in order to understand the nature of infection and the phenomena of immunity. It is this study that has ushered in the latest phase of our subject; and in this subject two names stand out particularly, those of Victor Vaughan and Abderhalden. Perhaps it would be equally correct to state that this latest phase corresponds with the study of anaphylactic phenomena, and of their relationship to immunity, for as I shall proceed to show, the two are most intimately connected.

If I may judge from the answers received this autumn from the candidates for Dominion Medical Registration, anaphylaxis is evidently regarded by the majority as one of those subjects that no fellow can be expected to understand; and addressing a general medical audience it is essential to describe its broad phenomena. Briefly, then, whereas, as everybody knows, the introduction of foreign proteins into the economy is in general followed by the development of immunity, the system gaining the power of rendering harmless many times the fatal dose of that protein, it is found that, employing minute doses of the protein for the first injection, if now, at the end of a week or ten days a second dose be injected, larger than the first, but still many times less than that producing serious symptoms on first injection, then instead of showing evidences of immunity, on the contrary the animal has become hypersensitive. It may, indeed, die within three to five minutes. In the guinea pig, which shows most strikingly these phenomena, there is an intense contraction of the muscular walls of the bronchi, whereby dyspnœa is brought about, with overfilling of the lungs so extreme that even when the chest wall is freely cut open immediately after death, the lungs remain expanded. With this there are muscular cramps and obstruction to the onflow of blood with capillary congestion leading to scattered hæmorrhages. This state can be induced by inoculation of any foreign protein, even one ordinarily

so harmless as egg albumen, or, on the other hand, by the employment of pathogenic bacteria and their proteid products.

Now here is the significant point. The symptoms and lesions produced by the poisonous moiety of split protein are, as Vaughan was the first to point out, identical with those seen in anaphylaxis. In other words anaphylaxis is due to the sudden setting free in the economy of the poisonous bodies of the same nature as the poisonous disintegration moiety of proteins. On the doctrine, therefore, that like results are produced by like substances, we arrive at the conclusion that this hypersensitiveness or anaphylaxis is essentially due to a disintegration of the introduced proteins with rapid liberation of the poisonous moiety.

But the first dose introduced sets up none of these phenomena, the second does. It is obvious that following upon the introduction of the foreign protein, the organism has gained a new power, that of splitting up the foreign protein.

It is at this point that Abderhalden's observations acquire a high significance. In 1910 Abderhalden with various pupils published a remarkable series of "serological studies by means of the optical method." Starting from the fact that the different proteins and peptones present each in the polariscope a specific index of rotation, he demonstrated first that, as determined by the polariscope, the ingestion through the alimentary tract of any particular protein has absolutely no effect upon the blood serum; its rotatory power is unaltered from the normal. But inject any of the more common proteins subcutaneously or directly into the blood, and in twenty-four or forty-eight hours remove some of the blood, separate the plasma, add to this a little of the protein, and now a remarkable change is seen: the index of rotation of the plasma undergoes progressive alteration, a clear indication that the protein is being broken down, and this is confirmed by the fact that by dialysis peptones can be separated off. In other words, within forty-eight hours after the introduction of a foreign protein, the system has responded either by elaborating a proteolytic or proteoclastic enzyme, or, it may be, by the rapid increase of production and discharge of already existing proteoclastic enzyme present in certain cells. What I would especially emphasize is the fact that the enzyme thus first liberated is not specific. It is an indifferent proteoclastic ferment: it will act not only on the particular protein inoculated, but on other proteins: it will break down indifferently globulin, casein, edestin, gelatin and their peptones, with the evolution of toxic peptone-like bodies.

It might be laid down that this indifferent ferment first produced is the cause of the anaphylactic phenomena. Against this view is the fact that Abderhalden's ferment is recognizable in twenty-four to forty-eight hours, whereas anaphylactic phenomena are not obtainable until the sixth to the tenth day. This in itself is not absolute disproof, for one of the factors governing the rate of enzyme action is the amount of enzyme present, and this might well depend upon the accumulation of a sufficient amount of the enzyme. The amounts should be large to cause dissociation of the foreign proteid at such a rate and such an extent as will lead to the production of symptoms.

There are, however, serious objections to this view. As pointed out by Abderhalden the anaphylactic phenomena are specific; it is only the protein first introduced that sets up disturbance; on subsequent injection other proteins are not affected, whereas Abderhalden's proteolytic and peptolytic enzymes are active in respect to any protein. The only safe conclusion is, therefore, that in these data we have evidence of the development of two stages:

1. Elaboration and discharge into the blood plasma, within forty-eight hours, of *indifferent* proteoclastic and peptolytic enzymes, affording Abderhalden's phenomenon.

2. The gradual production of more highly developed *specific* proteoclastic enzymes, having the power of rapid dissociation of the particular protein introduced, with liberation in the course of a few minutes of sufficient toxic disintegration product or products to set up symptoms.

I should note in passing that it cannot be regarded as absolutely settled as yet whether it is the enzymes liberated into the blood plasma that are the essential cause of the anaphylactic symptoms, or whether the phenomena are due to intracellular dissociation in specific groups of cells, such as certain cell groups and centres in the nervous system. If these cells under the action of the first dose have been stimulated to produce and consequently store the non-specific enzyme, the moment the foreign protein comes into contact with their cytoplasm, or is absorbed by them, it will undergo degradation. An extraordinarily minute dose of foreign protein in this way, by acting on, or being acted on by specific cells might set up fatal results. The rapidity with which anaphylactic phenomena may show themselves, and that upon the introduction of extraordinarily small amounts of any particular protein, rather favours the latter view: it suggests that there is a selective taking up of the protein by particular cells.

What I want to bring specially before you is that the two stages above postulated lead up to a third; in other words, that anaphylactic phenomena afford us explanation of the nature of immunity. By cautious reinjection of the foreign disharmonious protein we can pass through the anaphylactic to the succeeding stage of immunity. Now the characteristic of a true bacterial (as distinct from an antitoxic) immunity is that the body fluids gain remarkable digestive or fermentative powers. Any one who has observed Pfeiffer's phenomenon—has seen living typhoid or cholera organisms swell up and dissolve like pieces of sugar in the serum of a highly immunized rabbit or guinea pig—cannot fail to be impressed by the extraordinary digestive powers that have been acquired by the body fluids, through this process of immunization.

Everything here indicates that we deal with proteoclastic enzymes. Only now, in the immune animal, the process no longer leads to acute poisoning. I admit that more than one explanation may be sought and given for this fact, but choosing the simplest, we see here a further evolution of the same process, namely the development by the organism of further enzymes which disintegrate the poisonous moiety, and so carry on the degradation of the foreign protein to a further and harmless stage. It is pleasant to think that we owe to one of our own workers, Dr. Fraser B. Gurd, the first experimental evidence of the co-existence of these two orders of enzymes (lysins) in the immune animal*. As Dr. Gurd will show in his communication, it is not that the earlier enzymes are completely replaced: they are still active and indeed abundant, and evidence of the presence of these sensitizing bodies can be obtained in immune animals. But after they have broken down the specific protein with the production of the poisonous substance this is immediately acted on by the new enzyme and rendered innocuous.

To me it is not a little curious that Abderhalden, Thiele, and Embleton, and the other workers in this territory, while familiar with the existence of the great numbers of individual enzymes that are to be isolated from the organism, have not taken up and considered this probability of, or recognized the indications pointing to, the production of a succession of progressively more specific and more active enzymes in the development of the immune state.

Time forbids that I should deal with the nature of enzymes and the theory of their development. There is one point which before closing I must take up, namely, the nature of ectotoxins.

* *Amer. Jour. Trop. Dis. and Preven. Med.*, I, 1914, 776; *Jour. Med. Res.*, XXXI, 1914, 205.

In the first full study of these ectotoxins, that, namely, by Roux and Yerson a quarter of a century ago upon the diphtheria ectotoxins, it was clearly pointed out how many properties these bodies possess in common with the group of organic enzymes: their activity in extraordinarily minute doses; the impossibility of isolating them in a pure state; their destruction by a temperature of 60° Centigrade; their precipitation by phosphates and other salts. It is not a little interesting how notwithstanding bacteriologists in general have shown unwillingness to accept this view. Long years ago Sidney Martin in London brought forward further evidence to the same effect, that the diphtheritic membrane was not in itself highly toxic, that it contained an enzyme whose activity gave origin to toxic albuminoses, and that the internal organs, while showing no evidence of the toxin proper, might come to contain these toxic bodies. The significance of these observations lies in the fact that, as everybody knows, diphtheria bacilli are present in quantity in the membrane, and are almost absent from the internal organs. I have not come across a single leading German work on bacteriology that has taken any serious notice of these observations of one of the most brilliant and capable English workers. The stumbling block has evidently been in the prominence obtained by the phenomena of antitoxin production. This reactive production through the agency of ectotoxins of bodies which combine with the ectotoxins to render them inert, is wholly outside our usual conception of enzyme activities, and yet it deserves pointing out that, if we take solutions containing what we recognize as enzymes foreign to the animal body, enzymes, for instance, obtained from plants, and if we inoculate these into the animal body, anti-enzymes are developed identical in all their properties to the antitoxins. Dr. Zinsser of Columbia University in his excellent work upon "Infection and Resistance" which has just been published in the last few days, lays down that there is an important difference between ectotoxins and enzymes in their mode of action. He states: "while the toxins are apparently bound or neutralized by the tissues they attack, the action of an enzyme seems rather to be a process in which the enzyme unites with the substance it acts upon, is released as this result is obtained, and freed for further action without noticeable loss of quantity."

Here there is this very confusion that I have already noted, that, namely, of dwelling only upon the combination of toxin and antitoxin in the one case, and of the action of the enzyme upon the substrate in the other. Only two paragraphs lower down Zinsser

calls attention to the incubation period in the action of toxins, pointing out that this is longer when small doses are given, shorter when large doses are administered, but always evident. Thus in the horse he points out that it may be four or five days before the action of tetanotoxin shows itself: in mice, as De Waele points out, animals extremely susceptible to tetanotoxin, a minimal lethal dose gives an incubation period of thirty-six hours; if 3600 lethal doses be administered this is shortened to twelve hours, and whatever the dose, the interval cannot be shortened below eight or nine hours. Such facts as these cannot be explained as due to the activity of an ordinary mineral or alkaloid poison: ordinary poisons have no incubation period. It is wholly consistent with the action of a proteoclastic enzyme which, present in the blood or becoming absorbed by certain cells, by acting upon some specific proteid substrate, splits off a toxic moiety which, accumulating under the continued action of the enzyme, at length is present in sufficient amount to set up symptoms. The full proof of the enzyme nature of ectotoxins has recently been afforded by Abderhalden, who has demonstrated *in vitro* the proteoclastic properties of these bacterial toxins. In fact we must conclude that just as the animal body gives off free enzymes along the course of the alimentary canal, whereby foreign proteins of the foodstuffs are split up, and so made capable of absorption, so certain bacteria have a like power of discharging enzymes which can act upon the proteins of the animal economy and prepare them to be assimilated by the bacterial body, and it is in this process of disintegration of the proteins of the organism that the toxic moiety is liberated, thus inducing the symptoms of disease. It is these, and not the so-called ectotoxins, which are the immediate causative factor of this morbid phenomena.

Thus, to conclude, I would lay down the following as summing up the views here put forward as most satisfactorily harmonizing the data at present in our possession.

1. Whatever the nature of enzymes, the organism has the power of elaborating new orders of these bodies in and from its cells in response to the entrance into the tissues of foreign proteins, and potential food-stuffs in general.

2. The development of anti-bacterial immunity in an animal is essentially the development of the power of parenteral digestion of the constituents (mainly protein) of the pathogenic micro-organisms by the tissues.

3. This is rendered possible by the elaboration of a succession of (mainly) proteoclastic enzymes.

4. Three stages are to be recognized in this process:

(*a*) The development of indifferent proteoclastic enzymes.

(*b*) The development of specific proteoclastic enzymes, splitting the bacterial proteins into highly poisonous and non-poisonous moieties.

(*c*) The development of toxoclastic enzymes which render the disintegration products innocuous.

5. Ectotoxins are to the microörganism what discharged enzymes are to the animal. They have all the properties of enzymes.

6. They are not themselves toxic, but proteoclastic, and it is the products of their activity upon the proteins of the organism that are the essential toxic substances.

7. Antitoxic immunity is thus wholly distinct from antibacterial immunity. It is a process not primarily of digestion and disintegration, but rather of combination and fixation of enzyme, so that this is no longer capable of attacking and disintegrating successive complex proteid molecules, or, perhaps, of development of toxoclastic enzymes by the tissues, which disintegrate the toxic proteins as they are produced, rendering them innocuous or both.

THE Canadian Dental Corps in process of organization will be in command of Lieutenant-Colonel J. A. Armstrong of Ottawa. With him will be associated Major Gibson of Ottawa and Major A. A. Smith of Cornwall, together with twenty-four captains and twenty-four lieutenants. Several dental surgeons, who already have left for the front, will be attached to the unit when it arrives in England.

THE PHENOMENA OF ANAPHYLAXIS AND ALLERGY AND THEIR RELATIONSHIP TO IMMUNITY

By Fraser B. Gurd, B.A., M.D.

Montreal

THE discovery of the phenomena of anaphylaxis and allergy in 1906 has had such a vital influence upon the science of immunology that a proper conception of their nature is essential, if we are to be able to follow the recent and future advances in the knowledge of immunity processes.

In this short paper I shall attempt briefly to review the established characteristics of the two phenomena and indicate their relationship to one another and to immunity processes in general. In doing so I will adopt a frankly didactic rather than an argumentative or discursive attitude, in order that as clear a conception of the importance of these reactions may be obtained, as possible.

Should it prove desirable, the arguments supporting and opposing the views outlined can be considered in the discussion which is to follow.

By the term anaphylaxis (Richet) is designated the constitutional phenomena accompanying protein hypersensitiveness, while by allergy (von Pirquet) is meant the local or focal altered reactions which take place upon reintroduction of protein materials into sensitive individuals.

The experiments which are detailed in the following paragraphs exemplify certain of the more striking characteristics of the anaphylactic reaction.

If a series of half-grown guinea pigs each receive a dose of 0·2 cubic centimetres of sheep serum and subsequently be subjected to the following treatments certain striking and interesting results may be demonstrated.

G.P.A. may be given within five days of the first injection from 0·2 to 2·0 cubic centimetres of sheep serum without manifesting untoward symptoms.

Contributed to the symposium on Immunity, Montreal Medico-Chirurgical Society, December 4th, 1914.

G.P.B. fourteen days after the preliminary injection receives an intravenous injection of 0·5 cubic centimetres of sheep serum. Within a period of one or two minutes the animal will show evidences of grave irritation and will die within from three to eight minutes.

These manifestations consist of evidences of pruritis—scratching and sneezing; dyspnœa,—cough, cyanosis, slowed and forced expiratory effort with gradual cessation of respiration; nervous irritation,—convulsions and coma. Upon examination may be found drop in temperature, drop in blood pressure and leucopenia.

Immediate autopsy reveals the fact that the heart is still beating, the lungs are distended and present numerous hæmorrhagic areas, there may be marked splanchnic congestion.

The above may be looked upon as the typical anaphylactic experiment in the guinea pig and is known as anaphylactic shock.

G.P.C. is injected upon the same day as G.P.B. with an intraperitoneal dose of 0·2 cubic centimetres of sheep serum. There will be no immediate onset of symptoms, but within a period of one half to one hour the animal will be found to be suffering from malaise; the hair will stand on end and the pig will huddle itself in a corner and may shiver and be obviously unhappy.

The temperature will at first drop slightly and then show an elevation above the normal; a transient leucopenia occurs followed by leucocytosis. A scant purulent exudate may be recovered from the peritoneal cavity. The animal will recover within 24 hours.

We have thus discovered that if an animal which is susceptible to anaphylactic shock be given a *small* dose of protein a simple febrile reaction occurs.

Upon the following day G.P.C. is injected in a manner and with an amount of serum similar to G.P.B. No evidences of intoxication are found. This and other experiments prove that this animal has been desensitized; while in this state the animal is said to be refractory.

G.P.D. receives upon the fourth day after the original injection of 0·2 cubic centimetres an intraperitoneal injection of 2·0 cubic centimetres of sheep serum, and thereafter a like amount on three or more successive occasions at intervals of five or six days.

After a lapse of from twelve to sixty days after the last injection a dose similar to that introduced into G.P.B. is injected intravenously. No reaction takes place. If, however, a large dose, 3·0 cubic centimetres of sheep serum, be injected, typical anaphylactic shock with death will supervene.

This experiment demonstrates that an animal which receives repeated doses of protein remains hypersensitive to this protein, but that large toxic injections must be employed in order to bring about anaphylactic shock.

Another pig, G.P.C., fourteen days after the sensitizing injection of 0·2 cubic centimetres of sheep serum, is bled to death and its serum recovered. The serum thus obtained is injected into a normal pig with the result that the latter becomes highly hypersensitive. In order that such a transference of the anaphylactic state may be brought about, it is necessary to inject from two thirds to the total amount of serum recovered.

Similarly, if the serum of an animal treated in the manner of G.P.D. be injected into a normal pig, the latter becomes passively hypersensitive. It is found, moreover, that but a very small amount of serum, e.g., 0·1 cubic centimetre, is necessary.

The paradoxical phenomena are thus noted, that the serum of an animal, whose hypersensitiveness is easily demonstrated, contains but a small number of units of the anaphylactic body, whereas the serum of an animal in whom hypersensitiveness is proven only by the employment of large toxic doses of protein, contains a very large number, 100 to 200, or more, of units.

Obviously the animal D is not desensitized as was C, but has developed a state which may be described as immunity to the protein. At the same time it is noticed that *the more highly immune an animal may be, the greater is its potential hypersensitiveness.*

How, then, can the relationship of these two conditions of hypersensitiveness and immunity be explained? First, let us note that it is possible to transfer passive immunity to a normal animal by the employment of large doses, 2·0 cubic centimeters, of the serum from the repeatedly injected animal and also to confer immunity upon an actively sensitized animal such as G.P.B.

The sequence of changes which occurs in the animal's tissues is believed by the author to be somewhat as follows. Complex proteins, such as serum albumin, are not toxic to the tissue cells; they are, however, foreign and useless. The body, therefore, produces an antibody which acts upon the protein in such a way that a toxic substance (split-product) is formed. The animal whose tissues contain this antibody is then hypersensitive to such a protein. Reinjection of the protein in sublethal doses stimulates not only an increased production of the anaphylactic antibody but also a second order of antibodies which are able to neutralize or detoxicate the toxic product arising from the action of the first or anaphylactic antibody upon the protein.

The work of Vaughan, Abderhalden and others upon parenteral digestion makes it appear as if many, if not all, the phenomena of immunity may yet be explained in this way. If we attempt to bring the reactions of anaphylaxis into line in this fashion we have but to consider the anaphylactic body as being in the nature of a peptic ferment, and the second order, or immunizing body, as an ereptic ferment.

The peptic ferment reduces the protein to peptones and proteoses which are toxic, while the ereptic ferment causes cleavage of these substances, with the production of harmless or even utilizable peptids and amino-acids.

Allergy

When a normal individual is inoculated with smallpox virus a period of three days intervenes before an inflammatory reaction occurs. Once commenced this progresses for another week until an acute pustule is formed. If, however, the individual has been previously vaccinated, within a period of two years, the tissues react in a different fashion, hence, allos-altered, ergos-reaction, allergy.

In this altered reaction the hyperæmic stage is reached after the lapse of but a few hours, nor does it progress to a stage of pustulation, but is of short duration and does not go beyond the stage of hyperæmia with slight œdema.

The essential feature of this reaction is in the shortening of the incubation period. If the cells and vessels react soon after the introduction of the virus a less pronounced reaction will suffice to destroy the invader, since but little proliferation of the latter will have had time to take place.

This curtailing, or elimination, of the incubation period may be explained as follows: Morphologic tissue reactions—that is, vascular dilatation and cellular activity—occur only when the tissues are irritated. This may be demonstrated by the simple experiment of burying in the tissues two pieces of catgut one of which has been dipped in turpentine. At the site of the plain gut no reaction is noted, whereas an abscess forms about the turpentine-soaked gut. The vaccinia virus is essentially nontoxic and hence does not irritate the tissues. No reaction, therefore, occurs until such time as there has been produced in the tissues a body capable of so acting upon the virus that a toxic product is liberated. So soon as this toxic substance is developed the morphologic reaction commences, the de-

gree of reaction depending upon the number of units of virus which have been acted upon.

If it be borne in mind that of the two offensive methods at the disposal of the body whereby infection is overcome, cellular phagocytosis is much the more potent, granted that it may be induced to take place, the importance of the hypersensitive stage in stimulating the allergic reaction is manifest. *Under normal conditions protection of the individual against infection depends upon hypersensitiveness to the bacterial protein.*

The employment of bacterio-proteins or vaccines in prophylaxis or cure of disease is to be dealt with in other papers. Permit me, however, to indicate the problems which confront us in our efforts in that direction based upon our knowledge of anaphylaxis and allergy.

By means of the injection of bacterio-proteins or vaccines various results may be obtained, depending upon (1) the state of the individual injected; (2) the dose of bacterio-protein injected and (3) the interval allowed between injections. Thus any one of the following four alterations in the hypersensitiveness may occur.

1. Hypersensitiveness may be induced if such be absent, or increased if already present.

2. Hypersensitive individuals may be desensitized.

3. Both hypersensitiveness and immunity may be developed by means of repeated injections.

4. In chronically infected individuals where immunity suffices to mask their hypersensitiveness the immunizing bodies may be depressed so that their hypersensitiveness becomes more apparent and allergic reactions are stimulated.

5. Both sensitizing and immunizing bodies may be depressed to such a degree that all cellular and vascular reactions cease.

It is thus seen that in the employment of vaccines or bacteroproteins for clinical purposes we are, to say the least, dealing with a two-edged sword. In order, therefore, that favourable results may follow such inoculation procedures it is necessary that the physician know, relatively at least, the degree of sensitiveness of the individual to be treated and have a clear conception of the alterations, in the tissue and serum reactions, which he wishes to stimulate.

PROPHYLACTIC USE OF BACTERIAL VACCINES

By Lawrence J. Rhea, M.D.

Associate Professor of Pathology, McGill University; Director of the Pathological Laboratory, Montreal General Hospital.

THE use of what is known to-day as bacterial vaccine has come not from empirical reasons but from the application of scientific principles that have largely taken the place of empiricisms in medicine; from the practical application, both prophylactic and therapeutic, of scientific reasoning.

In discussing the prophylactic use of bacterial vaccines I shall refer to them in their broadest sense, regardless of their manner of preparation, save in the case of antityphoid vaccine, which to-day is so much before the medical profession as well as the general public.

Bacterial vaccines may be considered from two points of view, a technical and a therapeutic one. The technical procedures in their preparation are but means to an end; the production of a material that in its practical therapeutic application gives good clinical results. These technical procedures have been changed and improved from time to time, but, as they are of chief interest to the pathologist, I shall not go into their details. They all have been made with the view of producing a material whose therapeutic value is increased.

It is generally accepted that antigenic or protective properties of a bacterial vaccine are most efficient when the organisms which they contain are as nearly as possible in a living condition. The protective reaction in the body of an individual inoculated with such a vaccine should more nearly approach the protective reaction resulting from an infection with a virulent organism of the same kind.

What is attempted, then, is the production of a material which at the time of its therapeutic application will fulfil at least four conditions:

First, it must not contain any constituent or constituents which

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in properly regulated doses will produce detrimental lesions either at the point where it is inoculated or anywhere else in the body.

Second, it must not contain bacteria in such a state of viability as to make possible in any way their multiplication in the body and lead to an infection in the individual inoculated, or produce in them a state of bacterial carriers.

Third, the organisms should be in such a state that, should they accidentally come in contact with proper foodstuff, they will not multiply and thereby endanger the health of the community.

Fourth, they must contain certain constituents the reaction to which on the part of the individual inoculated will produce a body or bodies that will be antagonistic to the development of the same kind of organism in the body; that is, they must be efficient in terms of protective reaction on the part of the body.

The ideal bacterial vaccine, then, would be such a one as produces on the part of the body a reaction in every way similar to the virulent type of the organism from which it is prepared, save that there are no immediate and remote detrimental effects upon the body. The organisms in such a vaccine would have all the potential properties of their virulent brother save that they have lost their sting.

The prophylactic use of bacterial vaccines has been employed against a number of diseases of both man and the lower animals. The disease in man in which they have been used on the largest scale is typhoid fever. The beneficial results that have been obtained from antityphoid inoculation are familiar to you all, and I shall not refer to the convincing statistics upon the subject.

The recent work upon this particular prophylactic vaccine has dealt particularly with three points: first, the technical procedures in its preparation; second, the strain or strains of organisms to be employed; third, the number, size and interval of the dose to be given.

The technical procedure in the preparation of antityphoid vaccine has developed along three lines: first, the use of heat as a means of killing the organisms; second, the use of some substance by means of which they are sensitized; third, the use of some chemical substance or substances in killing them. In referring to these three points I shall not go into the details connected with each of them but shall discuss briefly some of the chief principles which underlie their application and some of their advantages and disadvantages.

The use of heat, within certain fairly limited degrees, produces

a vaccine the efficiency of which, in terms of protection to the individual inoculated, is well recognized. The temperature and the time it is applied has constantly decreased from above 60°C. for two hours to a temperature slightly above 50°C., for a period within an hour. The limits of 6° to 8° may make no great difference when applied for a few minutes but, when applied for an hour or more, lead to changes somewhat in proportion to the time it is applied. It is well known that the antigenic properties of bacterial vaccine are not thermostable, and heat above certain points or even lower temperatures applied over comparatively long periods destroy the essential constituents of a vaccine. The lower temperature applied to-day in the preparation of antityphoid vaccine means that one of the conditions to be fulfilled in the ideal vaccine is more nearly met; the typhoid bacilli in the vaccine used to-day are nearer the living organisms than they were a few years ago. The efficiency of such a vaccine has been proven by its use in the British and American armies.

There has been within the past few years a number of articles upon the strain or strains of B. typhosus that give the best results in terms of protective reaction. The principal ideas brought forth in these articles deal largely with three points: first, that a single properly tested strain is sufficient; second, that more than one strain, or a polyvalent vaccine, is best; and third, that typhoid vaccines should contain at least one strain of paratyphoid bacilli.

It is claimed by some that a vaccine made from a single strain of B. typhosus which has been proven to be efficient in terms of protective reaction, will protect against all other strains of this organism, regardless of their geographical location or their environment. Those who advocate the use of a monovalent vaccine do so for two principal reasons, a theoretical and a practical one. Theoretically, one might hold such a view upon the principle that the biological characters of B. typhosus vary but little in various parts of the world. I would not leave you with the impression that all cultures of B. typhosus are exactly similar biologically; much less would I have you apply such an impression to all other organisms, as for example, the gonococcus, where definite strains are known.

In practice the use of a monovalent vaccine gives sufficiently good results to be adopted by the British and United States armies. Nicholls of the United States Army covers the question well when he says that "heat-killed cultures are efficient, are safe, both as pertains to the individual inoculated and the possible infection of others." He does not claim that such a vaccine is the *summum*

bonum in antityphoid inoculation, though he does say, "improvements may be made, but before our results are improved upon they must be equalled."

Some workers advocate the use of a polyvalent vaccine and even suggest that such a vaccine should be made from organisms isolated from cases in the community where it is to be used. Such a vaccine would no doubt be efficient and under certain conditions its preparation might be practical, but it would involve considerable work, and could scarcely be applicable to the inoculation of armies, men, or bodies of men, who must be mobile.

The Japanese have recently advocated and have been using a typhoid vaccine to which has been added one of more strains of paratyphoid bacilli. Such a vaccine has the advantage that the individual inoculated with it should be protected from infection with both typhoid and para-typhoid bacilli. Para-typhoid infections are more common than we generally think, and protection against them should be offered.

The size, number, and interval of the doses of typhoid vaccine are fairly well established. The United States Army, where vaccination against typhoid fever is compulsory, has adopted the following: they give three doses at intervals of ten days; the first dose is 500m.; the second, 1000m.; and the third 1000m. The British Army on the other hand gives but two doses at ten days interval. The size of the dose is the same as in the United States Army. From a conversation with Sir William Leishman I take it that he believes in giving three doses but, as the use of anti-typhoid vaccine in the British Army is not compulsory, he is of the opinion that it is better, as yet, to give but two doses and have a comparatively large number of men receive it, than insist upon three doses and have a proportionately large number of men refuse to take it.

Sensitization of an organism means the exposure of that organism to the serum of man or some lower animal that has been immunized against the organism in question. Sensitized organisms may be used as such, or after they have been sensitized, may be killed by one of the methods referred to above. Sensitization of an organism does not kill it but takes from it the properties that make it infectious for the individual inoculated. Those who advocate the use of sensitized cultures are largely the French, where Beresdka has been especially influential. He advocates the use of living sensitized organisms largely from the results of His and Metchnikoff's experiments with inoculations of the higher apes with typhoid bacilli. These investigators succeeded in producing lesions in the

higher apes very similar to those found in man, and carried out experiments with the prophylactic inoculation of these animals against infection with typhoid bacilli. The result of their work, as it bears upon the question of prophylactic inoculation against typhoid infection, is briefly as follows: Heat-killed cultures, as they employ them, did not protect the higher apes against typhoid infection, while sensitized living cultures did. But too dogmatic conclusions can not be drawn from this work, since typhoid infection in the ape is both clinically and pathologically different from that in man.

It is probable that a living sensitized or a virulent culture is nearer the ideal vaccine than a killed culture. But in the light of recent investigations its use can not be said to be without dangers, not because there is any real danger to the individual who is inoculated with such a vaccine, but for at least two reasons: first, the possibility of carriers being produced; and second, the possibility of the sensitized organisms being given opportunity to become virulent. Recent investigations seem to show that certain lower animals may become chronic carriers of B. typhosus after inoculation with sensitized cultures of this organism. While this is denied for man until proof warrants its complete and unqualified acceptance, the use of such a vaccine should not be undertaken; there are too many carriers now to run the risk of producing even one more. If there is no danger to the individual inoculated with a sensitized vaccine, and no possibility of such an individual becoming a carrier, recent investigations have shown that conditions may arise whereby a virulent sensitized B. typhosus may become virulent. Sensitized B. typhosi, if planted upon artificial media, not only grow, but become virulent. A recent article from a member of the Medical Corps of the United States Army deals with a series of experiments bearing upon this point, and refers to the possibility of the containers of such a vaccine being broken in transit or in camp and the sensitized organisms which they contain finding suitable medium upon which to grow, thus making infection possible from them.

There is yet another method of preparation of anti-typhoid vaccine to which I shall only refer; a method whereby the organisms are killed with some chemical substance and the precipitated organisms suspended in some bland fluid, as normal salt solution.

There can be no doubt that typhoid vaccine offers a comparatively high degree of protection against typhoid fever. While this protection is not absolute, it is of a sufficiently high degree to warrant states, provinces, or municipalities assuming the responsibility

of preparing and distributing typhoid vaccine to its physicians. I see no reason why its preparation and use should be placed upon the same basis as smallpox vaccine.

Prophylactic Inoculation against Cholera: Since Ferron in 1885 first introduced prophylactic inoculation against cholera, considerable advance has been made upon the question. The earlier workers upon anti-cholera inoculation thought that it was essential to use a living culture as a vaccine. Haffkine's method of inoculation differed from Ferron's in that he used a greatly-attenuated culture at the first inoculation, and one of higher virulence at the second. Kolle has shown, however, that cultures killed at proper temperatures give as good results as living organisms. The statistics in regard to the protection established by using anti-cholera vaccine warrants its use in instances of probable epidemics. By the administration of properly prepared vaccine and the application of efficient sanitary methods, cholera should not be allowed to spread as it once did.

The use of living cultures of cholera bacilli as an anti-cholera vaccine has even more disadvantages from the standpoint of public health than those cited in regard to living typhoid bacilli.

Prophylactic Inoculation against Plague (applicable only in the Bubonic type). The statistics of Haffkine, who did the pioneer work on this question, are so striking that the efficiency of the inoculation can not be questioned. The comparative mortality among the inoculated and uninoculated is from 11 per cent. to 41 per cent. for the inoculated, and from 50 per cent. to 92 per cent. among the uninoculated.

Anti-Dysentery Vaccine. The difficulty in the application of prophylactic inoculation against dysentery has been due to the severity of the reaction following the inoculation. Dead cultures are so highly toxic that the general use of them has not been well received. A new technique in the preparation of anti-dysentery vaccine, which does away with the severe reaction following its administration, will, it is hoped, result in the preparation of a vaccine that will be of much use in preventing this disease. The principle underlying the preparation of this new anti-dysentery vaccine is one of sensitization of the organisms. Such a vaccine has no severe reaction following its administration. As yet no opportunity has presented itself for the employment of such a vaccine on a large scale. I saw last summer in Sir William Leishman's laboratory the first lot of this vaccine, made for distribution among the British troops then mobilized for war. Dr. Alcock, who per-

fected the technique of its preparation, informed me that the vaccine I saw was to be sent to France the next day, but it was not to be used unless an epidemic of dysentery developed among the troops. In the event of such a misfortune, it was to be administered at once. Let us hope that practical test of its efficiency may not be now.

Prophylactic Inoculation against Tuberculosis. Since the use of preparations of vaccines derived from the tubercle bacillus have been largely used as therapeutic measures, I shall refer to them but briefly. That an anti-tubercle vaccine is efficient in its protective powers, the work of Meakins has shown. He was able to immunize rabbits against virulent tubercle bacilli by inoculation with attenuated cultures. Barbour has developed a technique by means of which he is able to isolate a single tubercle bacillus. By this means he and Webb have successfully immunized monkeys against tubercle bacilli. The dose begins at one organism and increases. They have been able to establish an immunity in the guinea pig against the human type of this organism to a sufficient degree to protect the immunized animal against a sufficient number of virulent organisms of this type to kill 12,000 guinea pigs. They have inoculated two children of tuberculous parents without any signs of tuberculosis developing in the children. As Meakins suggested, the results of prophylactic inoculation against the tubercle bacillus are efficient and practical.

Prophylactic Inoculation against Whooping Cough. The work of Bordet and Gengou and others has been generally accepted as establishing B. pertussis as the etiological factor in this disease. There have been some attempts at prophylactic inoculation against this disease by the use of an anti-pertussin vaccine. The French claim good results, but I am informed by letter that the experience of some physicians in New York has not been so encouraging. I have been unable to find out how and by whom the vaccine they used was prepared. It is just as important in bacterial vaccines as in drugs in general to know that a vaccine to be used contains the proper organisms in the proper proportion and that it has been properly prepared. As an example I will refer to a letter from Dr. Theobald Smith of the Harvard Medical School, who informs me that he has had an opportunity of examining cultures of an organism used by a commercial firm in the preparation of an anti-whooping cough vaccine supplied by them, and that he has found that the organism used in this instance was not B. pertussis, but the closely allied B. bronchosepticus, the etiological factor in canine distemper and a pneumonia occurring in guinea pigs. These two

organisms are so closely related that they are distinguishable only by a few cultural reactions and by agglutination phenomena.

Prophylactic inoculation against Epidemic Cerebro-Spinal Meningitis. Sophian has shown that animals inoculated with a polyvalent anti-meningococcus vaccine develop protective bodies. There is reason to believe that such a vaccine would react similarly in the human and its use seems justifiable. This disease is not highly contagious, as only about 5 per cent. of secondary cases develop in houses in which it has appeared. It is well known that epidemic cerebro-spinal meningitis commonly appears among bodies of men, as armies that are massed together. Under such conditions a polyvalent vaccine would most probably be of benefit. It has been suggested that immune sera be given in conjunction with the first inoculation with anti-meningococcus vaccine. This is suggested on the basis that the passive immunity following the administration of specific sera should protect during the period immediately following the administration of the bacterial vaccine,—a period between the injection of the vaccine and the time when the body reacts to it in terms of protection. Such a procedure would seem especially advisable when dealing with physicians, nurses, and those who are exposed to the possibilities of infection at frequent intervals and over comparatively long periods.

In the animal world there are a number of prophylactic vaccines employed. I shall refer to but two of these, both of only recent application: a prophylactic vaccine against canine distemper and one against an epidemic type of pneumonia that develops in guinea pigs.

Prophylactic Inoculation against Distemper. Dr. E. Hamilton White has informed me of the attitude of one of the veterinary surgeons in Montreal in regard to the efficacy of the anti-distemper vaccine. He claims for it both preventive and curative properties.

Canine distemper is dreaded by dog fanciers and dog breeders. I am informed that the possibilities of young dogs contracting this disease interferes with dog shows and the field trials of sporting dogs. Canine distemper in a young bird dog may so greatly damage his sense of smell as to take a prospective fine field dog from field work and place him in the show class, or it may even ruin him.

Prophylactic Inoculation against Guinea Pig Pneumonia. There occurs an enzootic type of bronchopneumonia in guinea pigs that is quite fatal. We have lost fifty out of eighty pigs during one epidemic. Dr. Theobald Smith has shown that this disease is due to B. bronchosepticus, an organism closely resembling B. pertussis.

During the past winter our stock of guinea pigs was inoculated against this disease by the use of a vaccine prepared from a culture of B. bronchosepticus sent me by Dr. Smith. The entire stock was inoculated early in December, six weeks before the time the disease had developed in each of the past three years. No uninoculated controls were kept, so that definite conclusions as to the efficiency of the vaccination can not be drawn. It is encouraging, however, to note that we have not had an enzootic this year, the first year that we have not had at least one for four years. At a later date I hope to go into the question more thoroughly.

If one summarizes the present status of prophylactic inoculation with bacterial vaccines, there is abundant evidence to show that protection of varying efficiency may be obtained against a number of diseases. With the increasing application of newer technical methods of preparation the future of prophylactic bacterial vaccination is encouraging.

It seems unfortunate that prophylactic inoculation has been referred to as vaccination. To physicians it matters little whether it is referred to as vaccination or inoculation, but to the general public it is different. Vaccination to them means a procedure similar to that in smallpox vaccination with the sore arm and the resulting superficial ulceration. I have seen individuals who objected to anti-typhoid vaccination but gladly availed themselves of the opportunity to receive an anti-typhoid inoculation.

An amendment to the Medical Profession Act of Saskatchewan was read for the first time on May 25th. The purpose of the amendment is to establish reciprocal relations between the province of Saskatchewan and Great Britain. It provides that any person who is duly registered by the General Council of Great Britain may practise medicine in Saskatchewan upon payment of the necessary fees and production of satisfactory evidence that he is registered in Great Britain and of good character.

THE THERAPEUTIC EMPLOYMENT OF VACCINES

By J. C. Meakins, M.D.

AT the present time two separate and distinct methods of specific treatment of acute bacterial infections are in use. Either an immune serum, containing substances which render the infecting microörganisms comparatively harmless or neutralize their toxins, is administered; or an attempt is made actively to produce these immune substances in the human body by the use of vaccines.

Theoretically, both these principles are sound, and some very brilliant results have been obtained.

Unfortunately, many failures have been experienced, not so much on account of the fundamental principles being at fault as through trying to make all diseases conform to common modes of procedure. As time passes, it is becoming more and more apparent that the specific treatment of each disease must be worked out according to laws of its own.

As Dr. Rhea has pointed out, protection against certain diseases, such as plague and dysentery, was almost impossible by vaccination until the employment of the sensitized vaccines as prepared by Besredka. For many years it was held that the ideal method of vaccination would be living organisms. Now this is practicable, and the results are extremely encouraging.

It will be impossible for me to cover all the contributions on the specific treatment of infectious diseases which have been made in recent years.

First, a few words concerning the method of operation of vaccines and serums. A vaccine acts by stimulating the body to an increased production of protective properties against specific organisms or their products. The latter may be formed either during the process of growth of the organism, or after the death of the bacteria, when the protein of the bacterial body is split up into simpler but more toxic substances, such as albumoses or peptones. There has been no bacterium that I know of which has been proven to contain

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an endotoxin. It appears to me as reasonable to call the peptones derived from the digestion of beef, "endotoxins", as it is to call the split products of bacteria endotoxins. The only true bacterial toxins of which we know are those which are produced during the growth of the bacterium, as diphtheria, tetanus, botulismus, etc.

All curative sera are the result of vaccination, be it in the human or the horse. For instance, diphtheria anti-toxic serum is produced by vaccinating the horse with the diphtheria toxin. Many bactericidal sera have been produced in animals which have been successful experimentally, but have not given the results expected when used in human cases. The reasons for this are now being recognized.

In short, vaccination is the artificial production or stimulation of immunity in the patient during the course of the disease, while in sera we have preformed immune substances which act more or less as specific antidotes. Therefore, it may be stated that vaccines should be of most value in the treatment of the prolonged infections, such as furunculosis, chronic gonococcic lesions, whooping cough and typhoid; while serums should be especially efficacious in the treatment of the very acute diseases, as diphtheria, tetanus, pneumonia, and other streptococcic infections.

Whooping Cough. A few years ago, Bordet and Gengou described a bacillus associated with pertussis. This is very closely allied to the influenza bacillus in its cultural and morphological characteristics. But further experimentation has shown it to be a distinct variety unto itself, particularly so far as its immunilogical identity is concerned. Whooping cough is a disease especially suited to vaccination treatment on account of its prolonged course and notorious resistance to other forms of treatment. So very soon reports came from France, and later from other parts of Europe, and during the past year or so from America, of results from this method of treatment. As the majority of the cases were in children, small doses were used. The sensitized vaccine of Besredka was used in Europe, while the ordinary vaccines—killed by heat or phenol, have been used in America. The results are uniformly satisfactory, and with the sensitized vaccine, might be described as brilliant. An injection is usually given every fourth day, and after three or four doses, the cough disappears, and the patient remains perfectly well. As Dr. Rhea has intimated, a pertussis vaccine is now on the market: but if the result is not satisfactory, don't blame the method before you have ascertained that the organism used was really the Bordet-Gengou bacillus.

Typhoid Fever. Some years ago, I read a paper by Dr. Foster and myself before this society on the vaccine treatment of typhoid fever. Since then I have seen no reason to alter my favourable view concerning this method of treatment. The reports of others have been equally favourable, and its use is apparently becoming more and more general.

Typhoid fever seems to me to be particularly favourable for vaccine treatment. The onset is gradual, and a diagnosis can be made very early if modern methods are employed. But I wish to condemn the tendency there is to wait until the patient is in a very critical condition before vaccines are resorted to. During the first two weeks of the disease, typhoid bacilli circulate in large numbers in the patient's blood without producing any grave toxic symptoms. In the third week, they begin to disappear, and toxæmia of a more or less severe grade develops.

During these first two weeks, the body has been developing the power to digest the infecting organisms; during the third week, this digestion is very rapid, and the system is flooded with the toxic split products of the typhoid bacilli. Vaccination at this point is comparatively useless; in fact it is claimed to be detrimental. If vaccines, particularly the sensitized form, are used during the first ten days of the disease, the bacilli are destroyed more gradually, and a certain degree of immunity to the toxic products is developed. As a result of this early vaccination, the course of the disease is shortened, the toxic symptoms and prostration are lessened, the complications are fewer, and the mortality lower. I think that this is the most that could be expected of any method of treatment. It is not claimed that it is infallible, but it is certainly most encouraging. So much so, in fact, that vaccines should be considered a part of the routine treatment of typhoid fever as soon as a diagnosis has been made, and blood cultures should be used more consistently to attain this. Furthermore, vaccine treatment undoubtedly diminishes the frequency of relapses.

Gonorrheal Infections. For eight years, vaccines have been used with varying success in the treatment of gonorrheal infections. The chief objections to their use have been the violence of the reaction sometimes ensuing, the negative, and sometimes detrimental, effects in the acute stages of the diseases, and the uselessness of the treatment in the pelvic manifestations.

Recently the employment of sensitized vaccines has overcome many of these objections. Cruveillier and others have reported a considerable number of acute and chronic cases of gonorrhocal

urethritis, arthritis, orchitis and epididymitis, with almost uniformly good results. A general reaction sometimes occurred, with slight fever, but did not last more than a few hours: the local reaction at the site of inoculation was slight, and the discharge and signs of inflammation began perceptibly to disappear at the end of forty-eight hours.

The number of cases which have been reported by this method of treatment is not large enough to draw any sweeping conclusions, but the results are extremely encouraging, and hold out hope that a valuable remedial agent has been added to the therapeutics of gonorrhea.

Pneumonia. Pneumonia, on account of its frequency, high mortality and unsatisfactory treatment, early attracted the attention of those interested in immunity.

It is now over twenty years since patients were first treated by serum obtained from immune animals. The practical results were very disappointing. Although it has been impossible to show any marked lowering of mortality in any large series of cases as treated, yet careful clinical observers have been impressed by the improvement witnessed in individual cases. Moreover, it was early shown that suceptible animals might be rendered resistant to pneumococci, and also that a small amount of this immune serum would protect other animals for a short time. This experiment is so striking and fundamental that there is no wonder that efforts to find methods of using this serum therapeutically in man have been persisted in.

Neufeld has shown that a certain amount of serum in relation to the body weight is required to protect. On the other hand, a slightly smaller amount of serum will not protect against a much smaller amount of pneumococci. In other words, such a serum does not obey the law of multiple proportions, and to be efficacious even against a mild infection, it must be present in the body in a given concentration. Reckoning from his experiments on mice, at least 75 c.c. should be injected in man, and naturally much more after the infection has persisted for any time. It is evident, therefore, that one reason why anti-pneumococcic serum has not been more efficacious is that it has not been used in large enough doses.

Dochez has shown that there is a maximum degree of infection against which no amount of serum, however large, is able to protect. This suggests that to get the best results, the serum should be administered as early as possible before the infection has reached an extreme grade.

It is also necessary to point out the importance of being sure that the case being treated is caused by the pneumococcus, and not by some other organism, as streptococcus, B. influenza, Friedländer's bacillus, etc. In the past, anti-pneumococcus serum has been administered indiscriminately in all cases of pneumonia, no effort being made to determine in the individual case the nature of the bacterium causing the infection. As all immune sera are specific, it is seen that cases caused by organisms other than the pneumococcus would be uninfluenced by this serum. Furthermore, Neufeld found that an anti-pneumococcus serum would protect against the strain used for immunization, and also against certain other strains, but not against all.

Cole, recognizing these points as fundamentally important, proceeded to investigate different strains of pneumococci obtained from different cases of pneumonia. He found he could differentiate four types. An immune serum produced in a horse by a strain of Type I had a specific action against all members of the type, but had no action on the organisms of any of the other types. In a like manner, immune serum produced by the injection of a member of Type II was specific for members of this type only.

Type III was the so-called pneumococcus mucous. It was found impossible to produce an immune serum for this organism.

Type IV comprised all strains against which the sera of types I and II were ineffective, and which did not have the characteristics of Type III. Animals may be readily immunized to any member of this group, and the serum of the immunized animal is protective against the race used for immunization. In no instance, however, has this serum been found effective against any other race of this group, or against the organisms of other groups.

So far as cultural and morphologic characters are concerned, no constant group-differences have been discovered between the members of Group 1, 2 and 4. By means of the agglutination reaction it has been found possible to group the various races into types in exactly the same manner as by protection experiments.

In seventy-four cases of pneumonia studied, the number of cases found to be due to organisms belonging to each of the four types are as follows:

Type I.....	47 per cent.	65 per cent.
Type II.....	18 per cent.	
Type III.....	13 per cent.	35 per cent.
Type IV.....	22 per cent.	

It is now evident that in studying the effect of an immune serum on patients with pneumonia, but slight conclusions can be drawn from its indiscriminate employment in all cases. First we must know the type of organism used for its production; and second, it must be employed only in cases due to organisms of this type. So far it has been possible to produce a serum of high protective power against organisms of Type I, and a second serum—only slightly less efficacious—against organisms of Type II. It has been impossible to develop an immunity against Type III and in Type IV it would be necessary to immunize against every obtainable strain of this group. But the cases due to organisms of this type are comparatively benign.

The following table is given by Cole to demonstrate the relative virulence of each type:

Type I	24 per cent. mortality.
Type II	61 per cent. mortality.
Type III	60 per cent. mortality.
Type IV	7 per cent. mortality.

Type III, although very virulent, occurs as a causative agent in only 12 per cent. of the cases investigated.

Therefore, the problem resolved itself into treating the cases of pneumonia due to organisms of Type I and Type II with serum 1 and serum 2.

Immmediately the patient came under observation, the pneumococcus causing the infection was isolated from the sputum by injecting a small amount into the peritoneal cavity of a mouse, or by puncturing the lung (this procedure produced no ill-effects). However the growth of the organism is obtained, the agglutination test is at once applied. If not agglutinated by serum 1 or 2, it is useless to undertake serum treatment. If, however, one of the serums agglutinates the organism, treatment may be commenced at once with the appropriate serum.

Cole has treated seventeen cases with serum. The first dose was 50 to 100 c.c. diluted half with salt solution and injected into the vein. This was usually repeated in twelve hours and subsequent injections given as the condition of the patient indicated.

Fourteen cases were due to Type I and three to Type II. In the seventeen cases there were two deaths—mortality 14 per cent. as against 42 per cent. in untreated cases.

This is not a large enough series of cases to draw any conclusions

as to the efficacy of the serum as regards mortality, and other facts must be looked into. Likewise, the temperature charts are fallacious, although a general lowering of the temperature and a shortening of the course seemed apparent, and the lessening of the degree of intoxication was very manifest. More important than these clinical manifestations was (1) the disappearance of the organisms from the blood after the first injection; and (2) the appearance of immune bodies in the blood in considerable quantities after the first injection. These bodies do not appear in untreated cases until the critical fall in temperature.

In using anti-pneumococcic serum, three points are most important:

1. Early treatment,

2. Large doses of serum where it will have the best effect, i.e., intravenously,

3. Identification of the type of organism and the use of the appropriate serum.

Streptococcus. What has been said concerning the early work on pneumococcus immunity applies equally to the streptococcus. In the laboratory, anti-streptococcus sera have been produced for many years, and theoretically should be applicable to man. But a more careful study has shown that although a serum will protect an animal against the strain which has been used for the injections, it will not necessarily protect against other strains. Thinking to obviate this difficulty, sera have been produced by injecting into animals a number of different strains of streptococcus. As might be expected, the results have not been more encouraging than with the univalent serum. It is analogous to the old shotgun prescription. Without doubt, occasional very striking results have been obtained, even more striking than with anti-pneumococcus serum. Taking advantage of the specific immunity reactions which we find to occur amongst strains of the same types of organism, which cannot be differentiated by other means—as the pneumococci and meningococci—some advance is being made in separating the different strains of streptococci according to their phagocytic susceptibility. A serum produced by the injection of one strain of streptococcus, while it will promote phagocytosis of this strain, and perhaps several others, will not phagocytize the majority. As the degree of phagocytic power and protection go more or less hand in hand, future work may resolve the streptococci into definite immunilogical groups as found in the pneumococci.

In the meantime, anti-streptococcus serum should not be

ignored in treatment. It should be given as soon as a bacteriological diagnosis has been made. Also, the greatest concentration at the earliest time possible is always to be desired, and large doses (100 c.c.) should be given intravenously, as it takes 24 to 48 hours before a subcutaneous injection renders its full effect.

It must always be borne in mind that a serum must be active in order to produce results, and that some anti-streptococcus serums, which contain no anti-streptococcic bodies, have been found on the market.

As regards the treatment of streptococcus, blood infections by vaccines, but little success has been obtained by the ordinary methods. However, in the last two years several important series of cases have been reported where sensitized vaccine was used. The results were extremely good, especially those of Gordon (Bart's), who reports seventeen cases with five deaths; all of the mortalities had either meningitis, empyæma or peritonitis, or some combination. The twelve recoveries were all severe cases, in over half of whom the streptococci had been isolated from the blood.

Scarlet Fever. Of all the diseases that streptococci are associated with, scarlet fever is one of the most important. That streptococci cause it, there does not seem to be any definite proof, but that they are present as a very troublesome complication, must be admitted. Any reasonable attempt at the specific treatment of scarlet fever should be encouraged. During the past year, such attempts have been reported. Schultze of New York has described a micrococcus being always present in large numbers in the pharynx of scarlet fever patients. This organism he has called Micrococcus S. I will not discuss the bacteriology, but will briefly state the results as reported by Schultze and Goldberger.

A polyvalent heat-killed vaccine of streptococcus and micrococcus S. was prepared and given in doses of 400,000,000, and repeated in two days if necessary. One hundred and twenty-eight cases were treated, with a mortality of 1·5 per cent. The results observed after the inoculation were: a crisis in most of the cases within forty-eight hours, and almost uniformly a marked improvement in the general condition.

Keefer and Ferry, of Detroit, report one hundred and six cases treated in the same manner. The results are about the same.

Having no experience with this vaccine, I only mention it for what it may be worth.

The serum therapy of scarlet fever has seemed almost hopeless. Reiss has attempted a unique experiment. He does not approve

of the commercial serums for this disease (he is not alone in this): he urges the preparation of the serum on the spot in the laboratory connected with the scarlet fever ward of a public hospital. He has applied the method in forty severe and extremely severe cases of scarlet fever, including several children who seemed moribund. A sudden and complete transformation of the disease followed, convincing the most sceptical of the advantages of the serotherapy. The serum from at least three scarlet fever patients at the third or fourth week of the disease was mixed, and after adding five drops of a 5 per cent. solution of phenol to each 50 c.c., the ampulla was fused and kept on ice. The serum from each donor was tested for the Wassermann reaction and bacterial content beforehand. The dose for the serotherapy was 50 c.c. for a child and 100 c.c. for an adult, injected into a vein.

Tetanus. The prophylactic value of anti-tetanic serum is established. That tetanus anti-toxin properly used may save the life of a patient in whom tetanus has already developed, should be more generally recognised, and the treatment employed in every case at the earliest moment. Every hour lost before the giving of the anti-toxin decreases the chance of saving life. There is every reason to anticipate that with the proper use of anti-toxin, a mortality considerably lower than the present will be obtained.

It is important that the full effect of the anti-toxin should be obtained immediately, and this may be accomplished by giving large doses in the following manner: 3,000 to 5,000 units intra-spinally, and 10,000 to 20,000 units intra-venously, at the earliest possible moment—after symptoms of tetanus appear. On the following day, the intra-spinal injection may be repeated, and on the fourth or fifth day, 10,000 units should be given subcutaneously to maintain the anti-toxin content of the blood. This use of anti-toxin in no respect replaces other necessary recognized non-specific methods of treatment. Surgical treatment of the site of infection should be instituted at once, and all other well-known symptomatic treatment rigidly observed.

But the specific treatment of tetanus is of no value if the serum contains little or no anti-toxic properties. In 1906, Weaver investigated the therapeutic and protective value of the anti-tetanic serums on the market in the United States. His results were most astonishing. Many serums were absolutely useless; many more nearly so, and only a few were of any value whatever. Similar results were obtained with anti-streptococcus serums.

Our poor results in Montreal with anti-meningococcus serum

since the Rockefeller Institute has been unable to supply us, would substantiate this in another direction, while Dr. Rhea's reference to pertussis vaccine is a glaring instance of ignorance on the part of those who manufacture serums and vaccines.

Gentlemen, how is it that our government spends large sums of money to protect our sheep, and our pigs, and our oxen, and absolutely nothing towards the human animal? There is no inspection or control of biological products for human use in Canada; and furthermore, the medical profession as a whole does not seem to realize that this is most urgently necessary.

In closing, I would like to make the following suggestions:

1. The government supervision of serums and vaccines;
2. A more interested and charitable attitude towards this form of treatment by the profession;
3. Its early and energetic employment if it is going to be used at all, and not as a last resort.

THE following doctors have joined the Royal Army Medical Corps: Drs. E. B. Lang, R. E. Johnston, and F. Brodie, of Vancouver; Drs. J. S. Chisholm and W. P. MacKasey, of Halifax; Dr. H. M. Godfrey, of Marshfield, Prince Edward Island; Dr. S. R. Johnston, of Dartmouth, Nova Scotia; Dr. J. G. F. Heal, of Guysboro', Nova Scotia; Dr. H. S. Moore, of Kentville, Nova Scotia; Drs. Nathaniel Macdonald and W. W. Patton, of Cape Breton; Dr. G. W. Whitman, of Stellarton; Dr. Arthur Maxwell Fisher, of New Brunswick; Drs. Thos. F. Cotton, Fraser Gurd, W. S. C. Gowdey, A. M. Fisher, W. J. Grant, and R. R. Scott, of Montreal; Dr. A. J. Lomas, of Longeuiel, Que.; Dr. Ronald R. Scott, superintendent of the Western Hospital, Montreal; Dr. L. D. MacIntosh, of Hartland, New Brunswick; Dr. G. A. Ramsay, F. H. Bowen, J. Thornley Bowman, of London, Ontario; Dr. W. J. Hicks, of Wilkesport, Ontario; Dr. W. G. Laird, of Southampton, Ontario; Dr. C. R. Totten, of Windsor, Ontario; Dr. G. C. Bell, of Merlin, Ontario; Dr. G. C. Brink, of Port Stanley, Ontario; and Dr. T. P. Bradley, of Sarnia, Ontario.

FAT METABOLISM AND ITS RELATION TO ACIDOSIS

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THE first observations upon which our present ideas of fat metabolism are based date back as far as 1883 when Lebedeff[1] as the result of autopsies on patients who had died of phosphorus poisoning, noticed that emaciated subjects did not show that large amount of fat in the liver that is a normal characteristic of phosphorus poisoning. From this he was led to postulate that the fat in the liver was not formed on the spot from protein break-down, but came from the fat dépôts. It was a fat infiltration and not a fatty degeneration. This theory was put to the test of experiment. He filled the fat dépôts of dogs with an abnormal fat (linseed oil or mutton fat), then poisoned the animal with phosphorus and found that the liver contained the abnormal linseed oil or mutton fat in large quantities. This was a direct confirmation of his theory that the excess of fat in the liver as the result of phosphorus poisoning came from the fat dépôts. Though the work was not ideal from the chemical or experimental standpoint, it has been substantiated by all subsequent research and it is a testimony to Lebedeff's ingenuity that his technique has been followed until quite recently.

Rosenfeld,[2] in leading the attack of the Bonn school upon the Munich school of physiology, has widened and deepened Lebedeff's findings until they include an enormous number of cases in which the liver, heart and kidneys contain an excess of fat. Using dogs in which the fat dépôts had been filled with fat foreign to the animal, he proved an infiltration of the liver in phosphorus, arsenic and antimony poisonings, in phlorrhidzin and pancreatic diabetes, in chloroform, alcohol, and CO poisoning, and in the livers of geese prepared for the manufacture of *paté de foie gras*. In these cases the liver is infiltrated with fat from the fat dépôts: it is not "degenerated."

Read at the meeting of the Montreal Medico-Chirurgical Society, held on March 5th, 1915.

The next important step is due to Leathes[3] and his co-workers, Hartley,[4] Kennaway[5] and Meyer Wedell.[6] So far the assumption had been made that liver, heart and kidney fats were all of the nature of dépôt fat. Early investigations by Leathes[7] of the alcohol-chloroform extract of the liver showed that it contained large quantities—(40 per cent.)—of substances very definitely not fat. When these impurities were removed, the remaining substance, whether fat or fatty acid, was unlike that obtained from the fat dépôts.

Fat from the fat dépôts—the subcutaneous tissue, omentum, mesentery, adipose capsule of the kidney, around the optic nerve, and other nerves, and the pericardium—consists essentially of triglycerides of fatty acids such as palmitic, stearic and oleic acids. One molecule of glycerine combines, with the loss of three molecules of water, with three molecules of fatty acid to form one molecule of fat. The normal fats and oils of foods vary as regards the proportional amounts of the different fatty acids. Olive oil contains much oleic acid, lard less, and mutton-fat but about two-fifths. Butter fat is remarkable in containing a considerable percentage of fatty acids (butyric, etc.) volatile at the temperature of boiling water. The relative amounts of oleic acid can be gauged by the amount of iodine the fat can absorb. 100 grams of pure oleic acid can absorb 90 grams of iodine, and this figure is spoken of as its iodine value.

In general the fats of the fat dépôts are the fats of the foodstuffs eaten together with saturated fats manufactured from carbohydrates, so that each animal will have fats in its fat dépôts of an iodine value *below* that of oleic acid. But the fatty acids (and therefore the fats) of the liver, heart and kidney, have much higher iodine values. They are more unsaturated. 100 grams of liver fatty acids unite with about 135 grams of iodine.[8]

In this they are much more like fish oils and many clinicians assume that the value of cod-liver oil is due to these unsaturated fatty acids, and so reject Newfoundland cod liver oil, which becomes oxidised in its manufacture by exposure to air, in favour of Norwegian oil which is manufactured under an atmosphere of carbon dioxide. One fatty acid isolated by Hartley[9] from pig's liver (and presumably present in human liver) had before been obtained from fish and blubber oils only. Tissue fats, as opposed to dépôt fats, are unsaturated and oxidisable and closely resemble fish oils.

This discovery puts a simpler method in our hands of testing whether a tissue such as the liver is infiltrated with dépôt fat or not

If infiltrated, as the percentage of fat (or fatty acid) increases, the iodine value of those substances decreases. This has been shown to be the case in human livers by Hartley and Mavrogordato[10] in a series of analyses of material for the post mortem room, the iodine value bearing an inverse ratio to the percentage of the fatty acids. It has been confirmed by the writer working on bullock's liver and the clinching proof recently adduced by Imrie.[11] The last mentioned researcher constructs a theoretical curve on the following basis. He analysed a large number of human livers of patients from the General Hospital in Toronto, and found the average percentage of fatty acids and their iodine values in apparently normal livers. This forms the starting point of the curve. He then assumes that if the fatty acid doubles in amount, half will be from the fat dépôts and half that originally in the liver. The iodine value of fatty acids from the normal human liver is about 136; that from the dépôts 65. Theoretically, when the fatty acid doubles in the liver the new iodine value should equal $(136+65) \div 2$. When it trebles $(136 + 2 \times 65) \div 3$, and so on. It is easy thus to construct a theoretical curve. Taking the actual values in his analyses and comparing them with the curve theoretically obtained there is a remarkable correspondence between the two. This cannot be a chance correspondence and is undoubtedly to be regarded as a clear proof of an infiltration of the liver with dépôt fats.

But if we apply the same method of investigation to heart and kidney infiltrations we find no such correspondence between theory and fact. The iodine values actually observed are always higher than those theoretically deduced. The simplest interpretation is that the organs when infiltrated are infiltrated partly with dépôt fats and partly with fats that are already desaturated. Whence do the latter come? If we accept Leathes' theory of the function of the liver in fat metabolism[3] the explanation is clear. Leathes believes, and brings a number of cogent reasons to the support of his theory, that when fat is to be metabolised it proceeds first to the liver, there to be desaturated, and then on to the other organs to be utilised in the productions of energy.

On Leathes' view, as well as on Rosenfeld's,[12] the state of the liver when infiltrated, is physiological and not pathological. For this there is the morphological evidence adduced by the writer. In no case in the large physiological infiltrations observed has the nucleus of the cell suffered, although the cell may contain as many as seven fat globules, each as large as the nucleus.

This is further substantiated by the following argument:

The diseased states of the body that are accompanied by fat infiltration of the liver are very diverse and unlike. For instance, we may have it in diabetes, phosphorus poisoning, chloroform and alcohol poisoning, pernicious diarrhœa, stenosis of the pylorus, emaciation, etc., etc. *Where you have a symptom common to many widely different diseases, that symptom, however important from a clinical aspect, is not important as regards the etiology of the disease.* The excess of fat in the liver in these cases of fat infiltration is then a secondary phenomenon following on some primary disturbing factor. The common factor of the above pathological conditions is undoubtedly a disturbed or deficient metabolism either of protein or carbohydrate. In diabetes carbohydrate metabolism is disturbed; in poisoning there is excessive protein metabolism with wastage of tissue; in the other cases there is a real or virtual starvation of the body. In all cases, the fat reserves must be mobilized to supply materials for the production of energy and it passes first to the liver there to be desaturated. The fat is in the liver for physiological, not pathological, reasons.

Experimental proofs of this are to be found in work by Rosenfeld,[14] Leathes[15] and the author.[16] Rosenfeld finds that if and when he has produced a fatty infiltration of the liver by means of phlorrhidzin he gives the animal a meal rich in carbohydrates, the infiltration clears up within one day. This could hardly be the case if the infiltration denoted a pathological state of the liver. The author,[13] too, has found that whereas one day's hunger will cause the liver of Belgian hares to infiltrate, a second day's hunger will denude the liver of the infiltrated fat. Presumably the fat has been handed on, after a temporary sojourn in the liver, elsewhere. One day's hunger cannot be held to produce a pathological state of the liver especially as a further day's hunger brings the liver back to the normal morphological or chemical state. The same is true of the infiltration of the liver during late pregnancy and early lactation demonstrated by Coope and the writer[17] in rabbits. Only by a stretch of terms can that state be called pathological and there is no morphological evidence that the liver is then pathological. Similarly, in excessive fat feeding, the liver has been shown by Opie[18] morphologically and confirmed chemically by Leathes[19] and by the author,[20] to be infiltrated with fat. Whenever, then, there is abundant fat metabolism, the liver is found to be infiltrated with fats, presumably to be handed on elsewhere when worked up.

Recent unpublished work by Imrie, which he kindly allows the writer to quote, demonstrates the fact that the fœtus is greedy for

unsaturated fats and gives an explanation of why the liver is infiltrated in pregnancy. The material is being worked up for the benefit of the fœtus. That chick embryos utilize unsaturated fatty acids has been shown by Eaves[21] and by the writer[22].

The clinical bearing of this is obvious. Ordinary fat when the body is diseased, as in chloroform poisoning, has been shown by Opie[23] and Alford to be a dangerous food. When energy is wanted by the body in emergency as the result of some pathological condition it would be well to save the liver trouble by feeding with fish oils. Cod liver oil has already been shown to be useful in diabetes. But cod liver oil is not the only fish oil available. Sardines and herrings contain high percentages of unsaturated oils and have the advantage of being palatable though reputed to be indigestible. Fish roes contain fats[24] even more unsaturated, and there is metabolic as well as æsthetic grounds for the consumption of caviare. Fish oils we know are readily transported to the eggs of wild fowl for they are wanted for the nutriment of the embryo. Probably the same would happen, in view of Imrie's work, in pregnancy, and fortunately it does not matter whether or no the baby tastes of fish.

One subsidiary point of clinical importance seen in the work on pregnant animals' livers is that the infiltrations are greater if the animals investigated have but recently come from the vendor. Isolation, quietude and good dietary reduce the amount of infiltration seen at full term, suggesting that to the ordinary infiltration accompanying pregnancy there may be superadded an infiltration due to emotional excitement and a keen struggle for existence. This gives us an experimental confirmation of the well-known harmful effects of emotional disturbance during pregnancy.

The final portion of this paper has as subject the relation of so-called acidosis to fat metabolism. By acidosis, in its strictest sense, is meant an increase above the normal of acid (hydrogen) ions, in the blood. But it is generally used in the sense of an appearance of the acetone bodies (β hydroxybutyric, acetoacetic acid and acetone) in the blood with concomitant appearance of these substances in the urine. They are not present in the blood of normal adults, but in children they are frequently present to a small but definite amount.[25] But they are present in many diseases and may also be produced by experimental means. They are present in diabetes mellitus, sometimes the enormous amount of 100 grams β hydroxybutyric acid being passed a day.[26] They are present in chloroform poisoning, phosphorus poisoning, stenosis of the pylorus, hysterical vomiting, typhus and dysentery, etc., etc. In more

physiological conditions we find them during hunger, normal pregnancy, carbohydrate hunger[27] and excessive ingestion of fat; in fact in most of the cases in which the liver is infiltrated with fat. They are present, then, in widely different diseases and so cannot (by the criterion used above) be considered as anything but a secondary symptom of any of the diseases in question. From an etiological point of view they are irrelevant, though of great clinical importance. What is then the meaning of acidosis? If we compare the diseases and states of the body quoted immediately above in which we have acidosis, and those in which we have an infiltration of the liver it will be seen that they are practically identical one with the other. E.g. C H Cl_3 poisoning, diabetes, pregnancy and hunger are common to both sets. The occurrence of acidosis is parallel to the occurrence of fat infiltration of the liver. It is present when for any reason there is a large increase in fat metabolism and everything suggests that there is a causal relation between them—pancreatic diabetes in the dog being a possible exception.[28]

As Magnus Levy[29] has shown, in severe diabetes protein could not be the source of the acetone bodies. There was in his cases not enough carbon in the protein metabolized to account for the acetone bodies. It could not be from carbo-hydrate and must therefore be formed from fat.

Most amino-acids given to diabetics yield carbohydrate with the exception of leucin and tyrosin.[30] Saturated fatty acids (particularly butyric acid from butter) when given to diabetics increase the acetonuria.[31] When carbohydrate is cut out of the dietary the acetonuria follows, after a latent period of about six hours, the ingestion of fat.[32] In hunger, acetonuria becomes marked when the stores of carbohydrate are exhausted.[33] For these reasons it is clear that the normal source of the acetone bodies is to be found in fats.

Of the tissues that might be responsible the liver is found to be the only one which, on perfusion with fatty acids, yields acetone bodies,[34] consequently we must explain acetonuria as being due to an over-forced activity of the liver. It is suggested that the liver, not having sufficient time to desaturate the fats, breaks them down to β hydroxybutyric acid and acetoacetic acid in which form they escape into the blood, the acetoacetic acid spontaneously liberating acetone. Why the liver fails to complete the oxidation we do not know, but we do know that carbohydrates decrease acetonuria and that in acetonuria there is excessive fat metabolism.

If then we explain acidosis by overwork in fat metabolism on

the part of the liver, it would be well in such a case to ease off the work either by giving carbohydrates, which in many cases are efficacious, or, if these are contraindicated, by the use of fish oils. Much experimental work yet remains to be done on the oxidation of such oils by the body, but in the light of the work at present before the world, we may predict that they will be valuable in acidosis. Certain unsaturated acids, such as oleic and erucic, are said not to increase acidosis.

To sum up, we may say that in the light of our present knowledge, excessive fat metabolism is related with fat infiltration of the liver and with acidosis. The former is physiological and not pathological and is an expression of the function of the liver in fat metabolism: desaturation. The latter, acidosis, is the result of the fatty acid pursuing an abnormal path of metabolism, possibly as a result or overwork of the liver. In both cases increase of carbohydrate in the diet is advisable and, if these cannot be tolerated, fish oils, but not ordinary fats, are indicated.

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Case Reports

A CASE OF HÆMORRHAGIC CHICKEN-POX

By D. Grant Campbell

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THE following case is of interest on account of the rarity of the type and because there was an opportunity for a post-mortem examination.

M. S. was born on September 5th, 1914, and was admitted into the Montreal Foundling and Baby Hospital on September 15th following. On admission the infant appeared to be healthy except for a few skin blemishes, which disappeared rapidly under ordinary cleansing measures. She increased gradually in weight and strength and had the appearance of a healthy child. On January 2nd, 1915, a child was admitted to the hospital who two days later showed a typical varicellar eruption and was immediately isolated. The contagion spread, however, and most of the infants and one of the nurses have since acquired the disease.

On February 25th, 1915, M. S. gave the first indications of the disease (a few spots) and two days later the temperature rose to $102\frac{2}{5}°$, but fell to normal in less than twenty-four hours. On March 2nd, the temperature again rose suddenly to 102° and remained up till just before death. On March 3rd, at 9 a.m., the eruption became hæmorrhagic, the pustules forming the centre of small purple areas one-fourth inch in diameter. At the same time there was a slight vaginal discharge of blood (enough to stain the clothing) and at intervals all morning there was epistaxis, the blood being bright red. At 9 p.m. (twelve hours from the onset), a sharp hæmorrhage occurred from both mouth and nose, fully six ounces being lost. Various measures were tried to check the hæmorrhage with some temporary benefit and the baby rested quietly during the night but took no food, there being slight bleeding from the nose most of the time.

At 9 a.m., on March 4th, the child had a perfectly normal stool accompanied by a good deal of tarry blood, but no fresh hæmorrhage.

The baby died at 11.30 a.m., less than twenty-seven hours from the onset of hæmorrhagic symptoms.

Permission for an autopsy was obtained and Dr. Rhea kindly undertook it for us at the General Hospital.

The autopsy report is as follows:

The body is that of a fairly well-developed, but poorly nourished white female child, 60 cm. long. Rigor mortis is complete. There is very little post-mortem lividity. The pupils are equal and 5 mm. in diameter. There is no œdema. The superficial lymph nodes are not enlarged. The right external auditory meatus is normal. The left is filled with bright red clotted blood. Similar blood is seen in the nostrils. The skin shews lesions of irregular distribution, of various sizes, of different color and general character. The lesions are larger and most numerous over the back. There they vary in character, and representative types of the lesions found elsewhere in the skin are present over the back. The smallest lesions are seen as bright, small hæmorrhagic points, which are not elevated. On section, the hæmorrhagic area is very superficial. The remaining lesions vary in size to about the extent noted in chicken-pox. These lesions vary from 2 mm. to 1 cm. in diameter. They are all deep red, rather firm, and on section, contain a blood-tinged fluid. A few of the larger ones shew slight umbilication. On section, only the most superficial portions of the skin are involved. Besides these more elevated areas, there are a few lesions which are well dried up. Collectively, there are not over one hundred of the elevated lesions. (Specimen at McGill Museum.)

Peritoneal Cavity. The peritoneum is smooth throughout. There is no free fluid. There are a very few fine sub-peritoneal hæmorrhagic points, the largest not over 2 mm. in diameter. These are most numerous about the base of the mesentery on its inferior aspect.

Pleural Cavity. The pleura is smooth throughout. There is no free fluid. There are numerous very fine, sub-pleural hæmorrhagic areas, similar in character to the few already seen in the peritoneal cavity.

Pericardial Cavity. The pericardium is smooth. There is no excess of fluid. There are a number of small hæmorrhagic points under both the visceral and parietal pericardial layers, most numerous about the base of the heart.

Heart. Normal, save for the sub-pericardial petechia already mentioned.

Lungs. Normal, except for a few small sub-pleural petechiæ.

Spleen, Liver, Pancreas, Adrenals, Kidneys, Aorta, Genital Organs: No gross pathological lesions.

Gastro-Intestinal Tract. The œsophagus is normal. The mucous membrane of the stomach shews a very few fine red points similar to those seen in the skin and serous cavities. The remainder of the intestinal tract is normal. No hæmorrhagic areas or definite bleeding points are found. The lymphatic elements do not shew hyperplasia.

Head. The calvarium and scalp are normal. The dura is not abnormally adherent. There is no evidence of violence. The membranes are normal. The brain weighs 650 gms. There is very slight excess of apparently normal spinal fluid. There are a number of small hæmorrhagic points similar to those seen in the skin and serous cavities. These are most numerous about the base of the brain, especially in the inferior surface of the cerebellum. The mastoids are free from blood. Both middle ears and external auditory canals are filled with clotted blood. Both tympanic membranes are intact. The sphenoidal and ethmoidal sinuses are normal.

Anatomical Diagnosis. CHICKEN-POX, HAEMORRHAGIC, (VARICELLA HAEMORRHAGICA).

The chief features of interest are: (1) The rarity of the condition; (2) The serious prognosis; (3) The differential diagnosis.

The condition appears to be very rare considering how universal chicken-pox is. Allbutt's "System of Medicine"; Sir William Osler in his "Practice of Medicine" and Lockwood in his, are the only authorities whom I have been able to discover who mention it. In the literature there are a few cases on record, one of which is reported in the first number of the *British Medical Journal* for this year, in which case the child, aged three and one half years, recovered.

The prognosis is very grave and the few cases I have been able to discover nearly all ended fatally.

The differential diagnosis in this case was not difficult. It was one of an undoubted epidemic of varicella and the patient was kindly seen by Professor Blackader and Dr. J. E. Laberge (contagious diseases officer) who both confirmed the diagnosis.

Editorial

PATENT MEDICINES AND INFECTIOUS DISEASES

AT a recent meeting of the Ottawa Board of Health, when the question of the epidemic of diphtheria, then prevalent, was being discussed, one of the members of the board drew attention to the fact that a certain medicine called "Diphtherine," which was advertised as a cure for diphtheria, was being widely used. He suggested that in this epidemic it was partly responsible for the wide spread of the disease, four hundred and fourteen cases having occurred in six months. We feel that the point was well taken and that the sale of patent medicines professing to cure infectious diseases should be prohibited by law.

That the use of a patent medicine for the cure of infectious diseases must inevitably result, indirectly, in the spread of the disease cannot be questioned, when one considers the conditions under which this class of secret remedies is used. Recognizing the ease with which the exanthemata are transmitted, we have laws which make it compulsory to notify the public health officials of the existence of all cases of infectious disease in order that they may be quarantined, and the public guarded against their spread. But this duty of notifying the health department of his district of the existence of such disease, falls upon the doctor who discovers it; and the principal value of a patent medicine in the eyes of the ordinary layman lies in the fact that it enables him to dispense with the services of a physician. Is it to be expected that heads of families are sufficiently conversant with these laws to obey them? Even if they are, have they the special knowledge required to recognize these diseases in order to notify the proper authorities of their presence in the community?

Patent medicines are almost invariably cure-alls, and in most civilized countries now, including our own, the government undertakes to exercise some restriction over their indiscriminate sale by demanding that they be registered before they can be put on the market. A formula, giving the exact composition of each remedy, has to be submitted to the proper department, where the medicine is given a serial number and allowed to be sold, if it is found to contain nothing considered deleterious to health. This protects the public in a measure from dangerous drugs being dispensed in a secret nostrum. When, however, the use of such medicines endangers the health of the community at large, it is not enough to ensure that the so-called specific contains only harmless ingredients; the evil effects of its use in defeating the purpose of the laws aiming at the control of infectious disease must be taken into account, and this should be recognized and a licence refused for this reason.

When a patent medicine is used for a non-infectious disease, if it is worthless, as in generally the case, it does not increase the sum total of disease. The victims of misplaced confidence are the individuals who resort to its use and the general public does not suffer. There is then a vast difference between permitting the sale of an ordinary cure-all and a cure for infectious diseases.

That the medicine in question, Diphtherine, is harmless in so far that it contains no poisonous drugs, is evident from the directions given for its use. These state that it is to be used as a gargle only, except in the case of children too young to have learnt this method of cleansing the throat, when a teaspoonful is directed to be given internally every hour. On the other hand, the danger from its use by the public in general is enhanced by the fact that, though one is told how to recognize diphtheria clinically, the individual who has no confidence in his power to do so even with this help, has his difficulties solved by the statement that it is equally efficient and a sure cure for the sore throat of scarlet fever,

measles, whooping cough, croup, and other throat and lung conditions not of an infectious nature.

Can anyone believe that, recognizing the danger from such a course, the authorities would allow to be placed on the market a sure cure for smallpox? Yet these more common and less dreaded forms of the exanthemata kill their thousands to the few that succumb to smallpox.

TUBERCULOSIS IN CHILDREN

OF late years the suggestion that pulmonary tuberculosis in adult life is a recrudesence or lighting up, after years of quiescence, of an infection acquired during childhood, has been gaining more adherents. Belief in the possibility of the sudden outbreak of an old acquired focus of disease, years after it had ceased to manifest any clinical evidence of its presence, coupled with the almost universally accepted statement that as many as 90 per cent. of children at the age of puberty were infected with tubercle, tended to give force to this hypothesis. Hence, the recently published statistics of Veeder and Johnston, of St. Louis, which appear in the June number of the *American Journal of Diseases of Children*, are of interest, especially as they show a wide divergence from the results obtained by von Pirquet and Hamburger in Vienna.

The frequency of primary pulmonary tuberculosis in children under five years old has been a much debated question owing mainly to the evidence having to rest upon clinical signs and skiagrams. The presence of tubercle bacilli in the sputum cannot be determined for obvious reasons, and the interpretation of the physical signs and of the Roentgen picture is necessarily biassed by the fixed belief of the observer in the frequency with which this form of tuberculosis occurs in early life. In the diagnosis of doubtful cases one must be able to exclude the more common disease before one can conclude definitely that one is dealing with the less common.

It is true that in those cases where the disease has become dessiminated throughout the body, and has taken the miliary form, at autopsy the pulmonary lesions can often be shown to antedate those in other organs; but autopsies, except in such generalized cases, are not commonly obtainable. Clinicians agree that the utmost reliance can be placed upon the von Pirquet and tuberculin tests for determining the presence of a tuberculous lesion; but whether it is active, latent, or healed can only be decided by clinical examination. Any enquiry then into the proportion of children, other than those with known tuberculous disease, who give a positive reaction to these tests proves of value in determining the frequency of tuberculosis early in life in the cities of this continent as compared with those of the old world.

Working amongst the same class of patient as those from which the Vienna statistics were compiled, namely the, poorer classes of society, Veeder and Johnston obtained a very much smaller percentage of positive results. Of 1,321 children from a few months up to fourteen years of age, the percentage rises gradually from 1·5 in children under twelve months to 36 per cent, for the period of ten to fourteen years, when recognized clinical cases of tuberculosis are excluded; and to 44 per cent. when cases of clinical tuberculosis are included. Hamburger and Monti obtained a positive result in 94 per cent. of children between these ages and von Pirquet 80 per cent. though the latter used only the test which bears his name. As in both the Vienna and St. Louis cases all the children on whom the tests were made were in hospital for some pathological condition, the percentage of children in the whole community infected with tuberculosis is probably much less than these figures indicate.

DETERMINATION OF SEX

SELECTIVE reproduction was a simple matter to Deucalion and Pyrrha. Their method is set forth without impropriety in the school books. But so far both science and imag-

ination have searched in vain for the pebbles which they used. Plausibly infallible receipts for producing male or female offspring at will have never been lacking, but not one has long survived the test of independent research or unprejudiced practical application. The rules are empirical, and the data on which they are based are inaccurate or insufficient. Moreover, the uncertainty of so many factors such as the relation between ovulation and menstruation, and the interval between insemination and fertilization, leaves a loophole for escape from whatever objections may be urged against any hypothesis, which, in fact, nothing but a large body of reliable statistics could prove. After all, the chances of a successful prognosis of sex are mathematical, and practically even.

The modern scientific theories of sex fall into two groups, the physiological and the morphological. In the former group the nutritional theories are not at present in favour, but an interesting correlation of sex with metabolism is attracting attention. It is evident that throughout nature, male characteristics are preponderatingly active and catabolic; female characteristics on the other hand, are passive and anabolic. A book by Dr. T. E. Reed, published last year,* formulates an ingenious method of voluntary selection of sex on this basis. He has found that there is a definite lunar rhythm to be observed not only in menstruation, the classical example, but in many other functions, particularly in the fluctuation of the temperature and other symptoms in the course of the infectious diseases, and in the progress of labour. In labour the rhythm, Dr. Reed believes, is tidal, approximately six hours, a catabolic active period being followed by an anabolic period of rest. His obstetric records led him from this to the idea that the ovum has this same rhythm, and if fertilized during the catabolic phase, for instance, will result in a male. Moreover, these tidal periods are coincident in all persons in the same locality; conse-

*Sex: Its Origin and Determination. Rebman Company.

quently the theory can be put to the test; and the author claims to have had it tested successfully. In a word, prospective parents who may have a preference as to the sex of their offspring, are recommended to be ruled by the tide-tables for their latitude, if the intricacies of the more accurate Nautical Almanac are beyond their comprehension!

Passing to the morphological data, we leave the theories of voluntary selection and are on the more scientific ground of the biologist. But here, too, the findings of one observer contradict those of another, and what is true of many species does not always apply to another. Montgomery in reviewing the morphological data, which have accumulated rapidly of late, comes to the following conclusions: Each ovum has a prospective sex, which *may* be reversed by the entrance of the sperm. The sperm is thus a disturbing factor, sex-changing, rather than sex-producing, and probably acts by modifying the metabolism of the egg rather than by transmitting any particular sex-determinants. But what gives the ovum its prospective sex? From all this one is left with the impression that girl-babies will continue to be born, even in Asia, for many years to come.

It is the intention to establish medical boards in each divisional area of the country in connexion with the branch of the Militia Department charged with the allotment of pensions. In case of death, it is a comparatively easy matter to grant a pension as the amount is determined by the rank of the deceased and the number of those who were dependent upon him. In the case of disabled soldiers the matter is more difficult for the sum granted is then determined by the extent of the injuries received; this will be determined by the medical board.

A leper colony is to be established in Illinois at one of the State Hospitals for the Insane. Although there are only a few

cases of leprosy in the State of Illinois, some place is needed where persons afflicted with the disease may be isolated and properly cared for instead of being thrown into jail as has happened in certain cases. The decision to establish a leper colony is due largely to the efforts of Dr. Zellar, of the Illinois State Board of Administration.

THE vigorous measures taken in Serbia against the epidemics of typhus, relapsing fever, enteric, cholera and smallpox have met with such success that these diseases are now said to be almost stamped out. The origin of the typhus and relapsing fever infections was traced to Valjevo, where the diseases broke out among the Austrian prisoners. Hospital units were sent at once from England and from America to give assistance. On February 15th, the British Army Medical Service sent out a sanitary mission under Colonel Hunter and Lieutenant-Colonel Slammers. They proceeded to Nish and at once began to disinfect the hospitals and destroy lice; wine barrels were fitted up as disinfectors and distributed through the towns and villages; inoculation against cholera was carried out, and, wherever possible, bacteriological laboratories were established and investigation made of the sources of the various epidemics. Among other units sent were the Wounded Allies' Relief Hospital, the Scottish Women's Hospital, and that sent by the Serbian Relief Fund. Apart from the wounded, there were 37,000 sick in the Army, including 15,000 cases of fever, 8,000 of which were typhus, nearly 8,000 cases of relapsing fever, and 1,500 cases of enteric. In Kragujevatz, a town of 20,000 inhabitants, there were 1,400 cases of typhus, and in three months 3,400 deaths had occurred. At Nish, on April 5th, there were 8,198 cases of typhus in hospital; on April 18th, only 948. In the same period relapsing fever had declined from 7,693 cases to 4,861, and enteric from 1,443 to 1,126.

ACCORDING to a statement made by Mr. Tennant in the House of Commons on May 19th, the number of temporary commissioned officers in the Royal Army Medical Corps at that time was 3,100, irrespective of those who have recently taken commissions in the Territorial Force. Mr. Tennant also stated that nearly 6,000 medical men had been taken out of civil practice by the army. All senior medical students have been urged by the War Office to pass their final examinations as soon as possible so that they may be in a position to take temporary commissions in the R.A.M.C., and last winter a number of students who were serving in British hospitals in France were instructed to return home for their final examinations. In his address at the opening of the summer session of the General Medical Council, Sir Donald MacAlister said that enquiries at the several medical schools as to the number of students actually in attendance at the courses of medical study showed that the number was considerably over a thousand fewer than in 1913. Referring to the assistance given by the medical profession in the Dominions, Sir Donald said that Canada had been somewhat hampered owing to the fact that the registration laws of certain provinces had stood in the way of many able and efficient surgeons there resident who desired to come to the help of the Mother Country, but that the response to a communication he had addressed to the medical authorities of the provinces concerned, pointing out the imperial bearings of the question of reciprocity, had exceeded all expectations. From Ontario, British Columbia, Saskatchewan, Manitoba and Alberta, messages had been received, often by cable, stating that legislation had already been initiated for the removal of existing provincial restrictions. When the necessary steps were completed, all the provinces of Canada would have severally entered into reciprocal relations with the United Kingdom, and the way would be open for the application of the Medical Act, 1886, to the Dominion as a whole, as it is now applicable to the Commonwealth of Australia. (*British Medical Journal*, June 5th,

1915.) Reciprocal relations of course have already been established between the province of Ontario and Great Britain, and the necessary steps to this end have been taken by the province of Saskatchewan.

A JOINT committee upon the teaching of oto-laryngology in the medical course, and upon the training to be required of the specialist, has recently been appointed, to represent the American Otological Society, the American Laryngological Society, the American Medical Academy of Ophthalmology and Oto-Laryngology, the American Medical Association, and the American Laryngological, Rhinological and Otological Society. This Committee includes in its membership Dr. D. J. Gibb Wishart of Toronto, chairman; Dr. T. J. Harris, New York, secretary; Drs. Ballenger and Ingals of Chicago, Dr. Levy of Denver, Dr. Dean of Iowa City, Drs. McCuen Smith, Reber, Randall and Makuen of Philadelphia, Dr. Richards of Fall River, Dr. Chas. Richardson, Washington, and Dr. Birkett of Montreal. The Committee was organized in Chicago during the meeting of the Trilogical Society.

THE following is an additional list of contributions to the Fund for the Relief of Belgian Physicians and Pharmacists, received from members of the Montreal Medico-Chirurgical Society up to June 22nd, last: Dr. Thomas Gibson, $25.00 (Dr. Gibson also collected $172.00; the individual amounts were included in the list printed in the June issue of the JOURNAL): Dr. H. D. Hamilton, $25.00; Dr. J. A. Hutchison, $25.00; Dr. H. A. Lafleur, $25.00; Dr. C. F. Martin, $20.00; Dr. A. D. Blackader, $10.00; Dr. Marion Hansford, $10.00; Dr. E. J. C. Kennedy, $10.00; Dr. F. A. L. Lockhart, $10.00; Dr. I. C. Sharp, $10.00; Dr. J. W. Stirling, $10.00; Dr. G. G. Campbell, $5.00; Dr. A. Gould $5.00; Dr. E. S. Harding, $5.00; Dr. S. H. Martin, $5.00; Dr. H. S. Shaw, $5.00; Dr. J. W. Scane, $5.00.

Book Reviews

BLOOD-PRESSURE IN MEDICINE AND SURGERY. A GUIDE FOR STUDENTS AND PRACTITIONERS. By EDWARD H. GOODMAN, M.D., associate in medicine in the University of Pennsylvania. Philadelphia and New York: Lea and Febiger, 1914.

Much has been written about hypertension during the past ten years—many theories advanced to explain it, varied symptoms described as resulting from it, and an extensive and divergent therapy offered to combat it.

This is a book of two hundred and twenty pages well illustrated with charts, tables, and diagrams. The first two chapters are given to a review of the physiology of blood-pressure and a description of the methods devised for determining venous and capillary pressure. There is a chapter on instruments and methods for estimating arterial blood pressure; no mention is made of the Pachon Oscillometer, the instrument most used in France. Another chapter is taken up with non-pathological variations of blood-pressure. Ten pages on hypertensive cardio-vascular disease and hypotension are well worth reading.

In speaking of blood-pressure in renal conditions the author refers to Widal's classification based on the function of the kidneys. The two syndromes *chlorurémie* and *azotémie* should not be translated chloruremia and azotouremia; the French words simply mean chlorides and nitrogen in the blood. The author might in mentioning Widal's classification have included the hypertension syndrome, for Widal holds that hypertension plays a most important rôle in the symptomatology of nephritis. There is a whole group of symptoms resulting from vascular crises—numbness of the fingers, cramps in the calves of the legs, palsies and convulsions—the author should at least have referred to these. The final chapter is a review of our present knowledge concerning the effect of drugs and other therapeutic measures on blood-pressure. This book though it does not treat the subject of blood-pressure with any depth, will be found helpful to students and general practitioners.

Obituary

THE following appreciation of the late Dr. C. J. H. Chipman has been received from Dr. R. W. Powell, of Ottawa.

A familiar figure to the older generation of medical practitioners passed away at his home in Ottawa on Thursday, June 10th. Dr. Chipman was best known to McGill graduates and to those who obtained their early training in the Montreal General Hospital. Coming to Montreal in the early sixties, Dr. Chipman served his course through all its branches. His choice was McGill, where he graduated in 1868, and the Montreal General Hospital. There he was student, interne, apothecary, assistant surgeon and house surgeon, and derived inspiration from names that will go down to history in Canadian medicine, namely, Campbell, Howard, Fenwick, Drake, Reddy, Ross, Osler, and Roddick. These were the days long prior to trained nurses or antiseptics and the still greater triumphs of asepsis. To be a house surgeon in those troublous times meant more than can be explained—readiness and resource, alertness and quick wit and sound judgment, perseverance and integrity, deep reading and scientific investigation—these were all Dr. Chipman's, together with a kindly sympathetic manner and profound literary tastes. Later on, to be at work with those mentioned above—and then Shepherd, Cameron, Bell, Cline, Molson, Burland, Armstrong—names to conjure with in Montreal; to see Lister's and Pasteur's achievements exemplified at the bedside; to witness order and cleanliness brought forth from chaos: this was Dr. Chipman's portion. Still later, when in Ottawa—how shall we do him justice?—medical superintendent of the County of Carleton Hospital with Grant, Sweetland, Henderson, Church, Wright and Horsey, Powell and Cousens, Small and Jim Grant and Kidd to work with, appreciated by everybody, known to all—good deeds daily—no enemies, and a kindly nature, with literary tastes; of what need an obituary? His widow and surviving family of three sons and three daughters will be in the minds of many in Ottawa and the surrounding country in their affliction. A kindly personality and a sympathetic friend has been removed in Nature's good time. May he have the peace which passeth understanding!

DR. JOHN BLAIR GUTHRIE of Evanston, Illinois, died June 5th. Born at Guelph in September, 1868, Dr. Guthrie was educated at

Guelph and at Edinburgh, Scotland. He took his medical degree at Trinity Medical School, Toronto, in 1889 and in 1891 went into practice at Evanston. Dr. Guthrie leaves a widow, one son, and two daughters.

Dr. John Robertson McIntosh, of St. John, New Brunswick, died May 20th, in the fifty-fourth year of his age. Dr. McIntosh was born at West St. John; he attended the Grammar School there and in 1879 won the Corporation Gold Medal. In 1882 he obtained his B.A. degree from the University of New Brunswick. He then went to the University of Edinburgh where, in 1888, he obtained the degrees M.B., C.M.; two years later he received his M.D. degree. For a time Dr. McIntosh practised in Hartlepool, England; after that he spent about three years in London, paying particular attention to diseases of the eye and ear. He then returned to St. John, where he has been practising for the past twenty years. He leaves a widow and two sons.

Dr. William Wakeham, of Gaspé, died May 20th, in the seventy-first year of his age. Thirty-six years ago Dr. Wakeham was appointed by the Government fishery inspector for the Lower St. Lawrence and Gulf. The performance of duties connected with his appointment necessitated journeys to the Magdalen Islands and to remote villages along the north shore above the Labrador Coast; here Dr. Wakeham, as medical man and justice of the peace, made use of every opportunity of assisting the people and endeared himself to all. He was the representative for Canada on the Mixed Fisheries Commission. Dr. Wakeham was born at Quebec.

Dr. John E. McCuaig, of Erie, Pennsylvania, died May 18th. Dr. McCuaig was born in Oxford County, Ontario; he graduated from Queen's University in 1891. After practising for a time in Ontario, Dr. McCuaig went to the United States and was appointed to the staff of the State Insane Asylum at Danville, Pennsylvania. About twelve years ago he went into practice as a specialist in nervous diseases at Erie. He leaves a widow and three children.

Dr. P. G. Meldrum died of heart failure at Ayr, Ontario, on May 25th. Formerly in practice at Whitby, for the past few years Dr. Meldrum had been living at Toronto; and at the time of his death he was in charge of the practice of his brother, Dr. N. W.

Meldrum, at Ayr. Dr. Meldrum leaves a widow and four daughters.

Dr. James MacArthur, of London, Ontario, died suddenly from heart failure on Sunday morning, May 23rd, in the sixty-first year of his age. Born at Ailsa Craig, near London, James MacArthur, after completing his early education, entered Queen's University. After graduating in arts and medicine, he practised in London for thirty-five years, where he won both confidence and respect. Dr. MacArthur was one of the founders of the London Medical Association of which he was an active member up to the time of his death. For fifteen years he was a member of the Ontario Medical Council and a year ago became president of the Council. The duties connected with the presidency have been particularly onerous this year as a great deal of work was entailed in connexion with the establishment of reciprocal relations between Great Britain and the province of Ontario, the accomplishment of which was due largely to the efforts of Dr. MacArthur. The strain of his position, however, told upon him. His death is much regretted He is survived by two sons and three daughters.

Dr. William J. D. Sproule died at Harlem, Montana. He was a son of Mr. Newton H. Sproule, of Ottawa, and graduated from the University of Toronto in 1906.

Dr. Joseph Arthur Millette, of Megantic, Quebec, died at the St. Vincent de Paul Hospital, Sherbrooke, May 25th. Dr. Millette had been in practice at Megantic since April, 1884, and was well known throughout the district. He was born at Ste. Anne d'Yamachiche in 1860, and was a graduate of Laval University.

Dr. H. W. McGowan, of Knowlton, Quebec, died June 10th, at the age of seventy-one years. Dr. McGowan had practised in Knowlton for over twenty years.

Dr. George A. Stark died May 6th. Dr. Stark was born at Esquesing, Ontario, and was a graduate of McGill University. He practised in Milwaukee for eleven years, then went to North Dakota, where he built up a large practice in Morton County. He leaves a widow and seven children.

* Dr. J. H. Mathieson died suddenly on May 10th, 1914, in St. Mary's, Ontario, in the seventy-first year of his age. He was born in Embro, Oxford County, Ontario, where he received his early education. He subsequently attended Woodstock Grammar and the Normal School, Toronto. After teaching a few years he began to study medicine at McGill University, from which he was graduated as the "Holmes" gold medallist of his year, 1871. He immediately began to practice his profession at St. Mary's in partnership with his brother-in-law, Dr. Harrison. For thirty-one years he held a high and prominent position in medical circles. A particularly interesting case of his has been referred to by the late W. S. Playfair in his work on Obstetrics. Dr. Mathieson was a benevolent and public-spirited man and served St. Mary's for many years on the Council, Collegiate Institute and Public Library Board. He is survived by his widow and only son.

* Received from Dr. J. R. Stanley, St. Mary's, Ontario.

Dr. Charles Masson Gordon, of Kazubazua, in the Gatineau Valley, was one of the best-known and best-loved men throughout a district stretching from Hull to the River Desert and beyond. Born in Ottawa fifty-seven years ago, his early education was received there; later he entered McGill University. After receiving his degree in medicine, Dr. Gordon practised for a time in the west, but his life's work commenced when he went to the Gatineau. Here he won affection and esteem and an enviable reputation as a practitioner and a surgeon. He leaves a widow and five daughters.

News

ONTARIO

The following is a list of candidates who have passed the final examination of the College of Physicians and Surgeons of Ontario and are now licensed to practise: Joseph William Aikenhead, Brucefield; George William Alexander Aitken, London, Ont.; William Hambly Avery, Strathroy; Daniel MacTavish Baker, Fort William; Roy Ball, Toronto; Henry Merrett Barrett, Salford; John Arthur Bean, Clinton; George Ernest Binkley, Toronto; Robert Emmet Brady, Lindsay; Charles Oscar Broad, Little

Britain; Rufus John Whitby Brooke, Georgetown; Walter William Buttle, Cobden; Walter Ruggles Campbell, Toronto; Theodore Augustus Carpenter, Port Dover; William Allen Cathcart, Courtright; Charles Cecil Cornish, Ingersoll; Waring Gerald Cosbie, Toronto; James Henry Cotton, Toronto; Eldon Douglass Coutts, Toronto; John Grant Cunningham, Moose Jaw, Sask.; William Douglas Cruikshank, Hamilton; Gordon McIntyre Dale, St. Thomas; Allan Lester Delahaye, Pembroke; John Henderson Duncan, Toronto; I. De La Matter; George Percival Dunning, Riceville; Allan Boyd Earl, Athens; Wilbert Harold Eby, Cookstown; David Haynes Fauman, Rochester, N.Y.; Gordon Ferrier, Mimico; Robert Howard Fraser, Chatham; William Paul Freeman, Lucknow; Harry Garrett Furlong, Norwich; Leonard Albert Glenn, Adelaide; Edith Hamilton Gordon, Toronto; Thomas Fleck Graham, Brantford; Freeman Reginald Guest, London; Thomas Reginald Guilfoyle, London; Dan Henry Guy, Maxwell; Charles Augustus Harris, Lakeside; Joseph Wilbert Hayes, Peterboro; Percival Hearn, Toronto; Karl Edward Hollis, Hamilton, Bermuda; William Alfred Jones, London; Thomas Francis Kelly, Orillia; Harold Ivan Kinsey, Chatham; Heikki Koljonen, Port Arthur; George A. Lamont, Guelph; Edmond Larocque, Alfred, Ont.; Frederick Levi Leacock, Easton's Corners, Ont.; Frederick Winnet Luney, London; Joseph Alexander Macdonald, Toronto; Frederick Chas. Marlow, Blackstock; Ambrose Bell Moffatt, Toronto; George Monfette, Montreal, Que.; Walter Carneil Morgan, Arden, Ont.; Henry B. Moyle, Waterford; Authur James McGanity, Hamilton; George Crerar McIntyre, Paisley; John Judson McKendry, South Mountain, Ont.; William Russell McLaren, Corunna; Gordon Archibald McLarty, Toronto; David McMullen, Petrolea; Jonathan Foote McQuay, Toronto; Edgar Harold McVicker, Toronto; Robert White Naylor, Toronto; Chas. Newell, Milton; William Robert Newman, Toronto; Frances De Sales O'Connor, Harrowsmith; Vincent Keating O'Gorman, Cobalt; Arthur Allan Parker, Toronto; Gerald Hamilton Jeffery Pearson, London; Robert Wesley Phillips, Toronto; Adelard Louis Poisson, Belle River; Andrew Rutherford Riddell, Toronto; Thomas Clarence Routley, Toronto; Norman Franklin Schram, London; Thomas Jones Scobie, Hazeldean; William Glenn Siddall, London; Thomas John Simpson, Waldemar; Emerson Charles Smith, Chesterville; Melville John Sproul, Martintown; William Berkeley Stork, Toronto; Archibald Steinberg, Berlin; Henry Archibald Stewart, Saskatoon, Sask.; Valentine Frederick Stock, Tavistock; William Andrew Vanderburg, Cayuga; Stanley Arthur

Walker, Toronto; George McKee Watt, Brantford; Charles Edgar Wilson, St. Mary's; Ivan Dolway Wilson, London; William Nathan Winkler, Toronto; Harold Alonzo Wolverton, Nelson, B.C.

Thirty-six of the above candidates have obtained commissions as lieutenants in the Army Medical Corps and will leave shortly for the front. License to practise has also been granted to the following students who are already on active service. Thus, out of 133 successful candidates, 75 have already enlisted or intend to do so.

Gerald Allison, Picton; Robert Stanley Armour, Campbellford; Stanley Stafford Ball, Hanover; Arthur McKnight Bell, Merrickville; George Beatty Burwell, Renfrew; Leeming Anderson Carr, Hamilton; Harry Arthur Cates, Toronto; John Chassels, Toronto; Frederick Walter Clement, Deseronto; Richard Colter Coatsworth, Toronto; John Thomas Courtice, Toronto; Thomas Harold Crews, Woodstock; Charles Roderick Blackburn Crompton, Brantford; James William Deadman, Beeton; Donald Thomas Fraser, York Mills; Frederick Russell Gillrie, Hamilton; Morley Edward Gorman, Oakville; Harold Parrish Hamilton, Uxbridge; Maurice Round Helliwell, Toronto; William Roy Hodge, London; John Ranson Howitt, Hamilton; William Lorne Hutton, Brantford; Edward Shapter Jeffrey, Toronto; Clifford M. Keillor, Wallacetown, Frederick Russell Kirkham, Toronto; Herbert Carl Martin, Hamilton; Robert Beattie Martin, London; Athol Alexander Moon, Cotham; Robert Whiteman McQuay, Foxwarren, Man; Paul Michael O'Sullivan, Toronto; Samuel Alexander Overend; Caledonia; Reginald Paul, Sebringville; David Emerson Scott, Spry; Harry Roy Smith, Toronto; Thomas Harold Douglas Storms, Hamilton; Hermon Brookfield van Wyck, Chatham; Stanley Young Walsh, Peterboro; David Edmund Wishart, Toronto; Harry Wishart Whytock, Madoc.

An undue number of cases of smallpox continue to appear in the province. In May 55 cases were reported. They were from sixteen different municipalities. Other infectious diseases reported were: scarlet fever, 112 cases; 3 deaths; diphtheria, 191 cases, 13 deaths; measles, 659 cases, 9 deaths; cerebrospinal meningitis, 15 cases, 9 deaths; typhoid fever, 24 cases, 6 deaths; whooping cough, 39 cases, 5 deaths; tuberculosis, 114 cases, 81 deaths.

Dr. H. W. Hill has been reappointed director of the Institute of Public Health, London. Dr. Hill resigned the directorship of the Institute about a year ago in order to accept an appointment as Executive Secretary of the Minnesota Public Health Association.

DR. JAMES D. WILSON, of London, has been appointed physician to the jail in succession to the late Dr. James McArthur.

THE epidemic of diphtheria in Ottawa is reported to be well in hand. During the five weeks commencing May 4th, on which day Dr. Shirreff began his investigation, 57 cases were reported and two deaths occurred. During the preceding five weeks 73 cases and six deaths were reported.

MARITIME PROVINCES

THE hospital trustees have decided not to enlarge the Victoria Hospital, Fredericton, until more money is available for this purpose.

MANITOBA

THE infectious diseases hospital on Bannatyne Avenue, Winnipeg, has been converted into a convalescent hospital for soldiers.

DR. E. S. BOLTON, of Medicine Hat, Alberta, has been appointed medical health officer of Brandon.

SASKATCHEWAN

MEASLES and chicken-pox were unusually prevalent in the province during the month of May, the number of cases reported being, respectively, sixty-six and fifty-three, as compared with one case of measles and twelve cases of chicken-pox reported last year during the same month.

BRITISH COLUMBIA

DR. R. B. WHITE has been appointed medical health officer of Penticton in the absence of Dr. Channing-Pearce, who has left for England.

IT has been proposed by Dr. L. MacMillan that a bureau should be established in Vancouver for the purpose of collecting accounts rendered by physicians. At a recent meeting of the Vancouver Medical Association the proposal was discussed and it was decided that an outline of the plan should be sent to every practitioner in the city.

ARRANGEMENTS have been made whereby in the 1916-1917 provincial estimates $75,000 will be set aside as a building fund for the Vancouver General Hospital. The work of enlarging the hospital will be proceeded with at once.

THE provincial government will contribute $15,000 towards the building fund of the Royal Columbian Hospital at New Westminster. The sum necessary to complete the construction of the hospital is about $27,000 and the city of New Westminster will provide the balance, namely, about $12,000.

MEDICAL COLLEGES

McGill University

THE honorary degree of LL.D. has been conferred by the University upon His Majesty the King of the Belgians, "as a slight expression of the great admiration felt throughout Canada for the heroic courage and devotion with which he has led the people of Belgium in their resistance to an altogether unjustifiable, but evidently long premeditated attack on the integrity and independence of their country."

THE following appointments have been made in the faculty of medicine: Associate professor of pathology, Dr. Horst Oertel; assistant professor of chemistry, Dr. B. H. Krieble; lecturer in physiology, Dr. T. P. Shaw; lecturers in immunology, Dr. J. C. Meakins and Dr. Fraser B. Gurd; lecturer in hygiene, Dr. R. St. J. McDonald; lecturer in biology, Dr. F. S. Jackson; lecturer in general chemistry, A. R. MacLean.

Toronto University

The following is the list of those who recently graduated in medicine: William Harold Trevorrow Baillie, M.A., Toronto; John Arthur Bean, B.A. (Manitoba), Clinton, Ont.; Norman Edwin Betzner, B.A., Copetown, Ont.; Walter Ruggles Campbell, M.A., Toronto; James Henry Cotton, M.A., Toronto; Harold Dickson Courtenay, B.A., Ottawa; Eldon Douglas Coutts, B.A., Toronto; John Grant Cunningham, B.A., Moose Jaw, Sask.; Gordon McIntyre Dale, B.A., St. Thomas, Ont.; Joseph Daly, B.A. (Oxon.), Iona, P.E.I.; John Henderson Duncan, M.A., Toronto; Robert Howard Fraser, B.A., Chatham, Ont.; Edith Hamilton Gordon,

B.A., Toronto; William Thomson Kennedy, M.A., Toronto; David Easton Lang, B.A., Toronto; Ambrose Bell Moffat, B.A., Toronto; Vincent Keating O'Gorman, B.A. (Ottawa), Cobalt, Ont.; Andrew Rutherford Riddell, B.A., Toronto; Valentine Frederick Stock, B.A., Tavistock, Ont.; Roy Ball, Toronto; John David Henry White Barnett, St. Mary's, Ont.; Howard Black, Stroud, Ont.; Roy Armstrong Bond, Toronto; John Reginald Boyd, Meaford, Ont.; Charles Oscar Broad, Little Britain, Ont.; Walter William Buttle, Cobden, Ont.; Wyman Alexander Cameron, Advocate, N.S.; Theodore Augustus Carpenter, Port Dover, Ont.; William Allen Cathcart, Courtright, Ont.; Bessie Lawrence Collver, Waterford, Ont.; Warring Gerald Cosbie, Toronto; William Laurance Evans, Regina, Sask.; Leslie Clinton Fallis, Toronto; David Haymes Fauman, Rochester, N.Y.; Gordon John Ferrier, Mimico, Ont.; Thomas Edmund Peachey Gocher, Seattle, Wash.; Dan Henry Guy, Maxwell, Ont.; William Carroll Haney, Toronto; Robert Inkerman Harris, Toronto; Joseph Wilbert Hayes, Peterborough; Percival Hearn, Toronto; Arthur Belton Holmes, Toronto; Harold Ivan Kinsey, Chatham, Ont.; George Anderson Lamont, Guelph; Frank Lawrence Letts, Bridesville, B.C.; Albert George Ley, Markham, Ont.; George Chesterfield Livingstone, Toronto; Leycester Bancroft Lyon, St. Ann's Bay, Jamaica; Arthur James McGanity, Hamilton; George Crarer McIntyre, Paisley, Ont.; William Russell McLaren, Sarnia, Ont.; Gordon Archibald McLarty, Toronto; David McMullen, Petrolea, Ont.; George Walter MacNeil, Owen Sound; Jonathan Foot McQuay, Toronto; Edgar Harold McVicker, Toronto; Frederick Charles Marlow, Nestleton Station, Ont.; Harry Knight Mitchell, Port Arthur, Ont.; Robert White Naylor, Toronto; Charles Newell, Milton, Ont.; William Robert Newman, Toronto; Thomas Clarence Routley, Toronto; Thomas John Simpson, Waldemar, Ont.; Hildegarde May Smith, Bombay, India; William Berkeley Stark, Toronto; Vernon Harcourt Storey, Port Hope, Ont.; Frederick Henry Sutherland, Toronto; Stanley Arthur Walker, Toronto; George McKee Watt, Brantford, Ont.; Charles Edgar Wilson, St. Mary's, Ont.; William Nathan Winkler, Toronto.

No medals or scholarships were awarded in the faculty of medicine this year.

PROFESSOR IRVING H. CAMERON, who has occupied the Chair of Surgery at the University of Toronto since the year 1887, has been appointed honorary visiting surgeon on the staff of the King George Hospital, London.

Queen's University

No. 5 Stationary Hospital, which left for England a few weeks ago, under the command of Lieutenant-Colonel Etherington, is to be increased from 200 to 400 beds. The personnel also will be increased by the addition of four officers, four sergeants and thirty two rank and file.

Laval University

THE medical faculty of the University recently offered a military hospital of 520 beds for service overseas. The offer was accepted by the Militia Department on condition that the unit should be increased to a hospital of 1,040 beds. The University, however, has found it impossible to renew its offer for the present.

THE following candidates have graduated in medicine from Laval University, Quebec. Last year there were no graduates, as the medical course was then lengthened from four to five years. E. Perron, St. Charles; R. Beaudry, St. Raphael; J. M. Beaulieu, Sayabec; A. Desrosiers, Ste. Luce; J. A. Couture, Levis; J. B. Lacroix, St. Charles; L. Lizotte, Ste. Anne de la Pocatière; H. McCaffrey, Nicolet; J. A. Lafleur, St. Jean Deschaillons; R. Neilson, Quebec; M. Lavoie, Ste. Marie de Beauce; A. Tousignant, Ste. Sophie de Lévrard.

Alberta University

THE following physicians have been granted license by the University to practise medicine in the Province of Alberta: Dr. W. E. Fraser, Bashaw, Alberta; Dr. John Nay, Winnipeg; Dr. D. R. Wark, Mather, Manitoba; Dr. W. W. Inkrote, Diamond City, Alberta; Dr. E. A. Ferguson, Czar, Alberta. Supplementals have been granted to Dr. S. Astrof, Edmonton, in surgery; to Dr. J. E. Mason, Delia, Alberta, in anatomy and medicine; to Dr. E. F. Nivin, Jasper, Alberta, in anatomy.

Western University

THE annual convocation was held on May 28th, last, when the degree of M.D. was conferred by Principal Braithwaite upon George D. McTaggart, Gerald H. J. Pearson, Emmerson C. McFarlane and William M. Siddall. Degrees (in absentia) were also conferred upon Herbert R. Baines, Louis D. Chapman, Rupert G.

Doupe, M. Keillor, Irving J. Leatherdale, Wilfrid John Laurie, Beatie Martin, and David E. Scott. Drs. Laurie, Martin and Scott are serving in base hospitals at the front. The course in medicine at Western University also has been lengthened from four to five years and this is the last time that degrees will be given after four years of study. Dean McCallum announced that a campaign is to be undertaken this summer for funds to build a new medical building.

ARMY MEDICAL SERVICES

In a letter dated June 19th, just received from Captain James C. Fyshe, C.A.M.C., No. 1 Field Ambulance, First Canadian Divison, B.E.F., France, he states that during an action, when the wounded are coming in by the hundred, and the bustle, confusion, and dirt are at their height, and where there is no time to make up hypodermic solutions, the practice of administering morphine by placing a tablet beneath the tongue has not proved satisfactory, and that the use of "hypodermic units," each containing $\frac{1}{4}$ grain morphine and $\frac{1}{150}$ grain atropine, has given great satisfaction. It is likely that, with the approval of the Militia Department, an appeal will shortly be made for the necessary funds to defray the cost of supplying these "hypodermic units" to Regimental Aid Posts and Field Ambulances for use in emergency cases.

A clearing hospital has been established at Valcartier to receive wounded soldiers on their arrival from England. The patients will be examined and, if necessary, retained in the hospital until they are well enough to be moved to convalescent homes, or to their own homes.

Lieutenant A. L. McQuarrie has been appointed permanent member of the New Westminster Army Medical Examining Board in succession to Lieutenant J. W. Woodley.

No. 2. Clearing Hospital and No. 3 Stationary Hospital are stationed at Shorncliffe at the hospital which has been established there instead of the one at Bulford. Each unit remains under its commander, Colonel Rennie and Lieutenant-Colonel Casgrain respectively, but the hospital is under the command of Lieutenant-Colonel Wallace A. Scott. The patients in the various hospitals on Salisbury Plain have been removed to the Shorncliffe Hospital.

Dr. R. J. Manion, of Fort William, who has been serving on the surgical staff of an Anglo-French hospital established in the Chateau de Rimberlieu, near Compeigne, France, has returned to Canada but expects to leave again for the front very shortly.

Dr. J. G. McLeod, of Kincardine, Ontario, has joined the staff of one of the Red Cross hospitals in England.

Dr. A. D. W. Kay, of Fort William, has joined the French Army Medical Corps.

The following doctors who received their medical degrees from the University of Toronto before leaving with No. 2 Casualty Clearing Hospital, have been gazetted lieutenants in the Royal Army Medical Corps: Drs. Gerald Allison, Stanley S. Ball, Arthur M. Bell, Leeming Carr, Harry A. Cotes, John Chassels, Frederick W. Clement, Richard Collier Coatsworth, Thomas Harold Crews, Donald Thomas Fraser, Harold Parrish Hamilton, Maurice R. Helliwell, William Ray Hodge, H. Carl Martin, Athol A. Noon, Paul M. P. Sullivan, Harry R. Smith, Thos. Harold Storms, Stanley Young Walsh, and D. E. Staunton Wishart. Commissions in the R.A.M.C. have been granted to Drs. E. B. Lang, R. E. Johnston, and F. Brodie, of Vancouver; Drs. J. S. Chisholm and W. P. MacKasey, of Kalifax; Dr. H. M. Godfrey, of Marshfield, Prince Edward Island; Dr. S. R. Johnston, of Dartmouth, Nova Scotia; Dr. J. G. F. Heal, of Guysboro', Nova Scotia; Dr. H. S. Moore, of Kentville, Nova Scotia; Drs. Nathaniel Macdonald and W. W. Patton, of Cape Breton; Dr. G. W. Whitman, of Stellarton; Dr. Arthur Maxwell Fisher, of St. John, New Brunswick; Drs. Thos. F. Cotton, Fraser Gurd, W. S. C. Gowdey, A. M. Fisher, W. J. Grant, and R. R. Scott, of Montreal; Dr. A. J. Lomas, of Longueuil, Que.; Dr. Ronald R. Scott, superintendent of the Western Hospital, Montreal; Dr. L. D. MacIntosh, of Hartland, New Brunswick; Dr. G. A. Ramsay, F. H. Bowen, J. Thornley Bowman, of London, Ontario; Dr. W. J. Hicks, of Wilkesport, Ontario; Dr. W. G. Laird, of Southampton, Ontario; Dr. C. R. Totten, of Windsor, Ontario; Dr. G. C. Bell, of Merlin, Ontario; Dr. G. C. Brink, of Port Stanley, Ontario; and Dr. T. P. Bradley, of Sarnia, Ontario; Drs. W. G. Cosbie, E. D. Coutts, J. H. Duncan, P. Hearn, A. B. Moffatt, G. A. McLarty, E. H. McVicar, R. W. Naylor, W. R. Newman, A. R. Riddell, T. C. Routley, W. B. Stark, S. A. Walker, and W. N. Winkler, of Toronto; Dr. W. W. Buttle, of Cobden,

Ontario; Dr. W. A. Cathcart, of Courtright, Ontario; Dr. G. I. Dale, of St. Thomas, Ontario; Dr. G. Ferrier, of Mimico, Ontario; Drs. R. H. Fraser and H. I. Kinsey, of Chatham, Ontario; Drs. T. F. Graham and G. McKee Watt, of Brantford; Dr. C. A. Harris, of Lakeside, Ontario; Dr. J. W. Hayes, of Peterborough; Dr. G. A. Lamont, of Guelph; Dr. F. C. Marlow, of Blackstock, Ontario; Dr. A. J. McGanity, of Hamilton; Dr. G. C. McIntyre, of Paisley, Ontario; Dr. W. R. McLaren, of Corunna, Ontario; Dr. D. McMullen, of Petrolea, Ontario; Dr. C. Newell, of Milton, Ontario; Dr. V. K. O'Gorman, of Cobalt, Ontario; Dr. T. J. Simpson, of Waldemar, Ontario; Dr. C. E. Wilson, of St. Mary's, Ontario; Dr. C. O. Broad, of Little Britain, Ontario; Dr. J. G. Cunningham, of Moose Jaw, Saskatchewan; Dr. Melville Krolik, of Montreal; Dr. E. Vincent Sullivan, of St. Stephen, New Brunswick; Dr. Harry Lawson, of Rolling Dam, New Brunswick; Dr. H. J. Thomas, of Montreal; Drs. D. L. B. Wilmot and A. R. Thomas, of Winnipeg; Dr. J. C. Morris and T. J. Costello, of Calgary; and Dr. Henri Lasnier, of Montreal.

Dr. A. A. Mackay, of Montreal, has left for the front as medical officer to the 42nd Highlanders.

Major H. S. Muckleston, of Montreal, has been appointed sanitary officer at Valcartier, where part of the third and fourth contingents are now in training. The medical officer is Major G. A. Winters, A.M.C.

Dr. Young, of Ottawa, and Dr. A. A. Wilson, of Ladner, B.C., have left for the front.

Dr. Harold Williamson, A.M.C., of Port Arthur, has been gazetted Captain and will leave for the front with the field ambulance corps mobilized at Fort William.

Dr. J. E. McAskell, who for the past year has been resident physician at the Vancouver General Hospital, has left for France.

Captain D. Smith, A.M.C., of Stratford, Ontario, has been placed in charge of the field hospital of the 33rd and 34th battalions at the London concentration camp. Captain Smith will be in command of one section of the field ambulance which is to be mobilized in four sections.

After serving for some time with the Royal Army Medical Corps at Bethune, Dr. Streight, of Welland, Ontario, accepted a position on the staff of one of the London hospitals. He has now returned to the front.

Dr. M. J. Vigneux, of Nelson, British Columbia, and Dr. Stammers of Smiths Falls, Ontario, have joined the Army Medical Corps.

The following officers have joined the staff of the Canadian hospital at Le Touquet: Captain Jeffrey, Toronto; Captain McLean, Nova Scotia; Captain O'Hagan, Calgary; Captain Smith, Moose Jaw; Captain Flagg, Ottawa; Captain Dean, Winnipeg; Captain Panton, Vancouver; and Captain McEwen, Saskatoon.

Lieutenant-Colonel Harwood, of Edmonton, commanding officer of the 51st battalion, has left for the front. Captain Gunn accompanied the battalion as surgeon. Major Harris accompanied the 49th battalion in the capacity of surgeon.

Lieutenant J. J. Gillespie, A.M.C., of Pincher Creek, Alberta, medical officer to the 13th Mounted Rifles.

The following is the personnel of "A" Sanitary Section, A.M.C., which has been recruited at Montreal and expects to leave very shortly for England, where it will form a branch of the R.A.M.C. Officer in command: Major T. A. Starkey, of McGill University; Staff-Sergt. F. G. M. Williams, Corp. W. A. Brooks, Corp. R. W. Maynard, Lance-Corp. P. F. Seymour, Pte. D. Blunn, Pte. L. L. Brown, Pte. L. R. Bauset, Pte. W. B. Campbell, Pte. N. I. Chipman, Pte. B. Cooke, Pte. R. P. Cromarty, Pte. J. Dick, Pte. J. Duncan, Pte. K. H. S. Hague, Pte. E. W. Haines, Pte. W. G. Hardy, Pte. S. W. Harper, Pte. F. C. Hembling, Pte. R. W. Heward, Pte. J. A. Labelle, Pte. R. S. O'Meara, Pte. A. E. Pearce.

Captain J. H. Hamilton, of Revelstoke, British Columbia, has been appointed medical officer of the 54th Battalion, now in camp at Vernon.

The Vancouver military hospital will be known as No. 6 Canadian General Hospital and will be in command of Major E. C. Hart, chief of medical services in the province of British Columbia.

The personnel of the unit will consist of thirty-two medical officers, one dental surgeon, two quartermasters, two warrant officers, twenty-one sergeants and staff-sergeants, two buglers, two hundred and one rank and file, and seventy-three nursing sisters. About one-half of the personnel will be recruited in Vancouver. Among those who have volunteered to accompany the hospital are : Major F. C. McTavish, A.M.C., who served in the South African War and who took a prominent part in the organization of the eighteenth company of the field ambulance and commanded the section for several years. Major McTavish also took a prominent part in the organization of the St. John's Ambulance branches in the province of British Columbia. Dr. A. P. Proctor, chief surgeon of the Canadian Pacific Railway medical service; Dr. A. S. Monro, director of the Vancouver General Hospital; Dr. F. P. Patterson, Dr. J. W. McIntosh, Dr. A. B. Schinbein, Dr. C. S. McKee, Dr. J. S. Hogle, Dr. A. Rocke Robertson, and Dr. G. B. Murphy.

Drs. W. A. Clarke and Wallace Wilson, of Vancouver, have joined the A.M.C.

A hospital of 250 beds has been established at the Sewell camp, Manitoba.

A hospital of fifty beds has been opened at Three Rivers, Quebec, in connexion with the Montenegrin Reservists' Camp.

It is announced that No. 3 Canadian General Hospital (McGill) has arrived in France and is stationed at Camiers, the Boulogne base.

Dr. C. E. Bourne, medical superintendent of the Montreal General Hospital, has gone to Three Rivers, Quebec, where he has been appointed sanitary inspector of the camp. He is succeeded by Dr. E. T. Kirkland as medical superintendent of the hospital. Drs. E. Waterson and A. T. Bazin, of Montreal, have left for Valcartier.

Captain W. G. Cosbie, A.M.C., of Toronto, is attached to the 58th Battalion as medical officer.

Drs. F. W. Manning and Charles R. Totten, of Windsor, Ontario, have been appointed to the staffs of hospitals in France.

THE following members of the Army Medical Corps were mentioned by Field Marshal Sir John French for distinguished conduct in the field and their names appear in a supplementary list of King's birthday honours:

Temporary Colonel Gilbert Lafayette Foster, C.B.

Lieutenant-Colonel Frederick Sampson Lampson Ford, C.M.G.

Temporary Major H. A. Chisholm, D.S.O.

Captain T. H. McKillip, D.S.O.

Captain A. E. Haywood, awarded Military Cross.

Distinguished conduct medals have been awarded to Sergeant Brown, Sergeant-Major Clifton, and Private Turner.

The decoration of the Royal Red Cross is awarded to Matron E. Campbell.

Others mentioned by Field Marshal Sir John French are: Lieutenant-Colonels McPherson, Ross, Shillington, and Watt; Majors Duval and Hardy; Captains Bell, Brown, Donaldson, Fraser, McGibbon, McQueen and Stone; Quartermaster-sergeant Cooke; Staff-Sergeants Butt, Milborne, and Rotsey; Sergeants Brown, McKay (dead), and Smith; Corporal McDonald; Privates Bartley, Chester, Dalton, Farr, Holloway, Head, Lisney, Leishman, Millen, Stewart, Tompkins, Trottier, and Youldon; and Sister Richardson, of the Nursing Service.

THE Victoria Cross has been awarded to Captain F. A. C. Scrimger. Captain Scrimger, who is the son of Rev. John Scrimger, of Montreal, went to the front with the Fourteen Battalion. He is the first Canadian soldier to receive the Victoria Cross.

THE following have been transferred from No. 3 General Hospital (McGill) and have been given temporary commissions in the R.A.M.C.: Lieutenants G. F. Laing, of Windsor, Ont.; H. F. H. Eberts, of Victoria, B.C.; C. D. Kean, of Brockfield, Bonavista Bay, Nfld.; Otto Demuth, of Penticton, B.C.; P. B. Belanger, of Ottawa; L. H. Leeson, of Vancouver; H. F. MacNaughton, of Hopewell Cape, N.B.; A. D. Sharpe, of Summerside, P.E.I.; I. D. Ramsay, B.A., of Waskade, Man.; Wm. Templemon, of St. John's, Nfld.; D. Lee Smith, of Vancouver; F. S. Walcott, of St. James, Barbadoes, B.W.I.; C. O. Walsh, of Canso, N.S.; and H. C. Wert, of Avonmore, Ont.

DR. OSBORNE, of Hamilton, has been placed in charge of the eye and ear department of the Duchess of Connaught Red Cross Hospital at Cliveden.

TEMPORARY lieutenancies in the R.A.M.C. have been granted to the following who enlisted in the Canadian Army Medical Corps as non-commissioned officers or privates: Staff-Sergeants W. Deadman, S. Overend, D. A. Fletcher, G. M. Shaw, C. L. Arthur; Sergeant-Majors C. Brisco, W. Brown, Sergeants L. Carf, F. Overholt, J. Ryan; Corporals J. Williams, G. Burwill, E. Ward; Lance-Corporal J. Courtice; Privates J. Chassells, H. Oates, H. Murray, C. MacLean, H. Sharman, W. Pedlow, M. Van Duven, E. De Beaupré, F. Diamond, D. MacFarlane, H. McKenzie, K. Millan, J. Stewart, N. Glaoe, G. Cronk, J. Fisher, W. Clark, J. Box, A. Howson, K. MacKinnon and H. Jarman.

LIEUTENANT FRASER B. GURD, A.M.C., of Montreal, has been gazetted second lieutenant R.A.M.C.

CAPTAIN WILLIAM M. HART, C.A.M.C., of Regina, who was taken prisoner has been exchanged and has arrived in London. A tribute to Dr. Hart's bravery is paid by Mr. W. M. Scanlon, of Regina, who writes that in the middle of the terrible battle of Langemarck, Dr. Hart, scorning flying bullets and shrapnel, hurried to the assistance of wounded men in the face of almost certain death.

THE War Office has accepted the offer of the medical men of Vancouver to supply the personnel and entire equipment of a base hospital of one thousand beds. The offer made by the Saskatchewan College of Physicians and Surgeons has also been accepted. The unit supplied will take the form of a stationary hospital of two hundred beds with a staff of ten physicians, seventy assistants, one matron, ten nursing sisters, and sixteen staff nurses. It is estimated that the cost will be about $35,000.

CAPTAIN W. B. MACDERMOTT, A.M.C., of Lang, Saskatchewan, has been transferred from the 46th Battalion at Calgary to the First Canadian Mounted Rifles from Brandon.

CAPTAIN HAROLD B. BOYD, A.M.C., of Ridgway, Ontario, who was wounded while serving with the field dressing station attached to the fourteenth battalion, is home on sick leave.

Medical Societies

ONTARIO MEDICAL ASSOCIATION

THE thirty-fifth annual meeting of the Ontario Medical Association was held in Peterborough May 25th to May 28th, 1915, in conjunction with the annual meeting of the Medical Officers of Health. On Tuesday, May 25th, the fourth annual conference of the Medical Officers of Health of the province of Ontario was opened under the presidency of Dr. W. R. Hall, of Chatham. The attendance was good, about 280 members being present. At the morning and afternoon sessions several interesting papers were read, and in the evening the Mayor of Peterborough gave an address of welcome. The question of salaries for medical officers of health was discussed at the afternoon session on Wednesday and a committee appointed to consider the matter suggested the following schedule: townships, $300 per annum; incorporated villages up to 1,000 population, $150 per annum, with addition of $50 for each additional 1,000 population or majority thereof; towns, $100 for first 1000 population with the addition of $50 for each subsequent 1,000 population; cities under 20,000 population $1,000 per annum; cities of larger population $1,200 per annum. This schedule was adopted. It was pointed out that, in the case of towns and cities, the remuneration given should be sufficient to enable the medical officer to devote his whole time to the duties entailed by his position as medical officer of health. The election of officers resulted as follows: president, Dr. A. W. McPherson, of Peterborough, who is now on active service; vice-president, Dr. A. J. Macauley, of Brockville; secretary-treasurer, Dr. J. W. S. McCullough, of Toronto; committee on papers, Dr. Roberts, of Guelph, Dr. F. A. Dales, of Stouffville, and Dr. J. W. S. McCullough, of Toronto.

On Wednesday afternoon, a business meeting of the Ontario Medical Association took place, the president, Dr. D. J. Gibb Wishart, in the chair.

After the reading of the minutes, the following were elected to the nominating committee: Drs. H. J. Hamilton, J. H. Elliott, W. A. Young, A. Moorehead, F. C. Harrison, J. Loudon, N. D. Buchannan, H. B. Anderson, and W. H. B. Aikins. The following reports were then received and adopted: The Treasurer's, by J. H. Elliott; Audit by J. M. McColloch and E. A. Hammond; Credentials by

W. K. Colbeck; Papers and Business by H. J. Hamilton. At 4 p.m. the City of Peterborough and the local profession entertained the Association by an excursion over the Lift Locks, afterwards serving refreshments in the Armouries. The evening session met in the Collegiate Institute. The programme consisted of the President's address (see page 469 of the JOURNAL) and a paper on the clinical manifestations of syphilis, by Dr. J. G. Phillips, of Cleveland.

Thursday morning was taken up with the meetings of the sections in Medicine, Surgery, Obstetrics and Gynæcology, and Ear, Eye, Nose and Throat. In the afternoon, Professor F. J. Shepherd of Montreal delivered the address in Surgery; Dr. A. H. Wright gave a paper on Medical Education and Fee-Splitting, and Dr. A. F. McKenzie one on the local Medical Society. In the business meeting which followed, the Secretary read a report of the committee on the affiliation of the County Medical Societies which recommended the following:

1. "That a member should belong to a local Society before becoming a member of the Ontario Medical Association, special provision being made for admission for members living in districts not yet organized.

2. "Membership in a local Society makes a member eligible for the Ontario Medical Association and his fee may be collected through the local Society.

3. "It shall be the duty of this committee to obtain the volunteer services of members of the Association to aid the organization of societies."

Dr. H. J. Hamilton presented the report of the Committee on the relations of the Ontario Medical Association and the Canadian Medical Association, reporting progress and asking leave to sit again. After some discussion these reports were adopted.

Resolutions:

Moved by Dr. Bruce, seconded by Dr. H. J. Hamilton, that the Association have a paid organizer for the coming year. Carried.

Moved by Dr. C. Myers, seconded by Dr. Hamilton, "That this Association desires to place itself on record in favour of active steps being taken immediately for the prevention of insanity by the establishment of separate neurological wards in general hospitals, especially in those hospitals in which clinical teaching is given." Carried.

The Nominating Committee then presented its report:

Place of meeting, Toronto; President, Dr. H. B. Anderson; vice-presidents, Drs. G. S. Cameron, Peterborough; A. T. Emmerson,

Goderich, C. B. Oliver, Fort William; W. K. Colbeck, Welland; general secretary, Dr. F. Arnold Clarkson; assistant secretary, Dr. F. C. Harrison; treasurer, Dr. J. H. Elliott; delegates to the Canadian Medical Association, Drs. D. J. Gibb Wishart, F. C. Neal, and H. J. Hamilton.

Moved by Dr. J. H. Elliott, seconded by Dr. W. A. Young, that the usual honorarium be paid the secretaries. Carried.

Moved by Dr. Elliott, seconded by Dr. F. N. G. Starr, "That we, the members of the Ontario Medical Association, assembled in anuual meeting wish to express our deep appreciation of the loyalty and self-sacrifice of our fellow members of the profession who have offered themselves and are now serving the Empire and its allies at the front in the various services. In thus serving the cause of freedom, many will come back under conditions which will practically mean beginning their professional life over again. As fellow practitioners, we wish to assure them that as far as lies in our power, we will see that their old clientèle awaits them on their return to civil practice, and that their relations to former patients will as far as possible be restored. For the fulfilment of their arduous duties, we wish them health and strength, and we express our sincere hopes of a speedy and safe return to their homes and families." Carried.

The following resolution was passed unanimously by the section of Obstetrics and Gynæcology: "That the general session appoint a committee to consider and enforce adequate measures for a campaign amongst the members of the medical profession and the public to guard against the ravages of cancer, by early diagnosis and treatment; and to report at the next meeting of the Ontario Medical Association." Carried.

Moved by Dr. Colbeck, seconded by Dr. N. D. Buchanan, "Be it resolved that this Association deplores the fact that very inadequate provision has been made for the payment of medical and hospital fees of workmen injured in the industrial concerns of the province. While some manufacturers, in addition to their contribution to the funds of the Compensation Board, have made ample provision, many others have done nothing whatever. We would ask that the Compensation Board take steps in co-operation with the Government, to have amendments made to the Workingman's Compensation Act, so that workmen, who received only half pay while incapacitated, will not be under the necessity as at present, of paying these charges out of their already too-scanty earnings." Carried.

Moved by Dr. A. A. McDonald, seconded by Dr. H. B. Anderson,

that a hearty vote of thanks be tendered to the Mayor and Council of the City of Peterboro, and to the Ladies' Committee, for their great kindness and hospitality to the members of this Association, and that a copy of this resolution be sent to the Mayor. Carried.

The new officers were then installed.

The evening session was held in the Collegiate Institute.

On Friday morning sectional meetings were held in the Armouries. The total registration was 176.

MONTREAL MEDICO-CHIRURGICAL SOCIETY

THE ninth regular meeting of the Society was held Friday February 5th, 1915, the President, Dr. W. F. Hamilton, in the Chair.

PATHOLOGICAL SPECIMENS: Series by Horst Oertel, M.D.

1. *Large liver abscess of obscure origin and etiology.* The patient, a man thirty years of age, entered the Royal Victoria Hospital apparently suffering from an acute infectious disease, which originally was diagnosed as probable typhoid fever. This, however, was soon questioned. He presented more or less indefinite abdominal symptoms and, at first slight, and later more accentuated, pulmonary symptoms, pointing to the presence of fluid in both chests and rather indefinitely to cavitation. The Widal reaction was negative, white blood cell count 17,600, temperature varied from 98° to 104·2° with a pulse of from 76 to 140. Urine concentrated with a slight amount of albumen, no casts. The disease ran in a general way the course of a septicæmia.

Autopsy disclosed double exudative fibrinous pleurisy, both lungs floating in a large amount of turbid fluid. The lungs showed multiple abscesses. The right lung contained four or five intercommunicating small abscesses in the middle lobe, with similar ones in the lower and upper part of the upper lobe. Some were also in the lower lobe near the base. There existed a certain amount of purulent infiltration of the lung tissue immediately surrounding these abscesses. The left lung showed only one or two small abscesses in its upper lobe. There was nowhere extensive pneumonic consolidation, save that limited purulent infiltration of lung tissue surrounding the just-mentioned intercommunicating, apparently metastatic, abscesses.

Searching for other foci, attention was immediately directed to the tremendously enlarged liver, which had pushed the dome of the diaphragm on the right side upward, although the liver itself was

quite free from it and not adherent. On the left side, the liver had been pushed by this enlargement of the right lobe upward and backward, so as to reach the dome of the diaphragm on the left side and resting against the spine. However, it was everywhere free from adhesions. The structures of the portal spaces were free, portal glands not prominent. The portal vein and the vena cava inferior contained fluid blood and were otherwise unchanged. The enlargement of the liver was almost entirely at the expense of the right lobe, the upper part of which was extremely bulging and on percussion fluctuated. This enlargement of the right lobe was responsible for the displacement of the rest of the liver substance to the left, upward and backward. The weight on removal was 4,075 gm. On section a tremendous amount of creamy, greenish, but non-odorous pus escaped from the upper part of the right lobe and it was found that the largest part of the upper lobe, leaving only about 7 cm. of the right lower lobe, was transformed into intercommunicating abscess cavities. The whole of the right lobe of the liver measured, after removal of the pus, 25 × 17 cm. The left lobe to the interlobar notch measured 10 × 15 cm. The left lobe was flat and apparently quite uninvolved. A further examination of the iliac veins and the inferior vena cava, as well as the carotid arteries and the aorta, showed these vessels only filled by fluid blood. The mesenteric glands were not prominent. The stomach, duodenum, gall-bladder and ducts were free. Nothing of any further importance was discovered at autopsy and section had been limited to abdomen and thorax, so that other structures in this regard important, as, for instance, the middle ear, could not be examined. Under the circumstances, it is not easy to trace the origin of the lesion and determine its etiological factor.

In the first place, the bacteriological examinations, kindly made by Dr. Bruère and Dr. Mason, were interesting, but not conclusive. During life, the pleural fluid was found sterile and non-pathogenic to mice and guinea pigs. At autopsy, some of the pus from the liver abscess and some from the lung was examined with the following results: In the lung were predominatingly hæmolytic and non-hæmolytic streptococci, two diphtheroid bacilli, a few definite pneumococci and organisms of very similar morphology to those which were practically pure in the liver abscess. These latter were gram-positive diplococci growing in staphylocoid masses. They were not capsulated and were impossible to cultivate ærobically and anærobically on media containing blood serum. This organism was found non-pathogenic for mice and guinea pigs. The

bacteriological examination, therefore, leaves the etiology rather misty.

Tracing now the origin, it appears from examination of the liver, particularly where the lesion is still more recent, that the extension within the liver corresponds to what is usually characteristic of a portal infection. As is well known, infections of the liver may enter through the bile ducts, the lymphatics, both of which could be easily ruled out in this case, or the vascular system. Of these ports of infection, the venous system is, of course, the most important. This may be concerned either through the portal system or by retrograde infection through the hepatic veins. It was, as will have been seen, perfectly impossible to trace any portal infection in this case. There existed no ulceration in the gut, mesenteric arteries and veins were perfectly intact and, as previously recorded, all the structures of the portal spaces were free. The question arises, therefore, whether it is possible in this instance to deal with an arterial infection or one through the medium of the hepatic veins. Now, infection through the hepatic artery rarely produces extensive large abscesses in the liver. It is most frequently encountered in septic endocarditis and then usually produces small miliary abscesses, but this does not correspond at all to what we have here before us. There remains, then, the possibility of infection through the hepatic veins by retrograde embolic metastases from a distant focus. In middle ear disease it is, for instance, possible that bacterial emboli may reach the jugular vein, the superior vena cava, the right auricle; travel backward through the inferior vena cava to the hepatic veins, thence to the liver, where they primarily form small embolic abscesses. But these, in breaking down, may involve, and then extend within, the portal system of the liver, thus gradually simulating a true portal infection. In other words, the picture of a portal infection in the liver may result from a general bacteriæmia, and I am inclined to believe that this is what occurred in this case, although original focus and port of entrance remain obscure. As to the direct etiological factor, we are, of course, unable to make any statement with any definiteness, but there is some foundation,—not much, but some,—that the case belongs to the category of pneumococcic pyæmias. What bacteriological evidence we possess, further the character of the pus, and, finally, past experience are in its favour. It is certainly most peculiar and interesting that this diplococcus stained exceedingly well but resisted all attempts at cultivation and had lost all its pathogenic power. If it, therefore, belongs to the group of pneumococci,

or, indeed, under any circumstances, it is certainly a very attenuated organism which must have lost its pathogenic property in the develo ɔment of the disease.

2. *Carcinoma of cervix extending to parametrium.* This second specimen is an extensive carcinoma of the cervix, inoperable at the time of admission to the Royal Victoria Hospital, which illustrates exceedingly well the progress of this disease. The specimen shows the cervix absolutely destroyed, necrotic, in process of cavitation; but one also sees that growth and ulceration stop abruptly at the body of the uterus. The disease does not extend upward beyond the cervix, but sideways into the right parametrium, producing a similar extensive ulcerative growth. Within the parametrium it has travelled upward so as to involve the right ovary and right tube, leaving the body of the uterus intact. Thus the progress of this carcinoma is not one by continuity or even contiguity, but by preference typical of lymphatic extension. The case was complicated by involvement of the ureters, leading to their dilatation and an early hydronephrosis.

3. *Complete tuberculosis of both supra-renal glands, communicating with vein on left side, miliary tuberculosis, no Addison's disease.* In a case of miliary tuberculosis of both lungs, complicated by tuberculous meningitis, was found a very advanced cheesy tuberculosis of both supra-renals. In the left super-renal practically no normal tissue remained. Sections of what might grossly still be regarded as a remnant of supra-renal tissue in the upper pole, show even this transformed into tuberculous cheesy masses. A larger vein is found to communicate directly with the cheesy masses in the centre of the gland, so that, undoubtedly, a ready access was established to the rest of the circulation. The right supra-renal was not quite so diffusely affected, but nodular masses also permeate it very generally. This case is not only interesting as illustrating a rare origin of the miliary tuberculosis, but because symptoms and signs of Addison's disease were lacking entirely. In this connexion, however, one anatomical peculiarity of the case is interesting: the surroundings of both supra-renals were free. As is well known, immediately beneath them lies the solar plexus with a rich sympathetic system. In the majority of cases of tuberculosis of the supra-renals, associated with Asddion's disease, they are found to involve, by adhesion or extension, the underlying sympathetic system. Whether this absence had anything to do with a lack of development of Addison's syndrome in this case can, of course, not be definitely stated, but a record of this observation seems worth while. Earlier ob-

servers of Addison's disease, as, for instance, Virchow, were inclined to attribute much greater significance to the involvement of the neighbouring sympathetic structures than to the supra-renal itself, and Virchow stated that other lesions in the situation, as inflammations or growths from the stomach or glands might be associated with Addison's syndrome, if they affected this sympathetic plexus. Later investigators have, however, denied this and attributed the disease to an interference with the internal secretion of the supra-renal gland. It seems difficult to see how any secretion could have been continued in this case. No other, accessory, supra-renal glands were found at autopsy. One must, therefore, suppose that other parts of the chromaffinic system compensated.

DEMONSTRATION of lantern slides illustrating diseases of the auricle with electro-cardiograph charts, by Dr. J. C Meakins.

DISCUSSION: Dr. T. F. Cotton: These slides of Dr. Meakins are of particular interest to me, and I am sure to all of us who are interested in heart work. The newer methods of examining the heart tell us a great deal about the significance and nature of disorders of the auricle and the important rôle they play in producing heart failure. Perhaps there is no alteration in the mechanism of the heart that is of more interest to the clinician than great acceleration of the auricular rate, both as an explanation of the symptomatology and as an indication for treatment with drugs of the digitalis group. As Dr. Meakins has shown, there is a very close relationship between auricular flutter, premature auricular contractions, and auricular fibrillation. In many cases the onset of the auricular flutter is preceded by individual isolated premature auricular contractions for a period of months. A large number of cases of auricular flutter, certainly the majority of those which we treat, terminate in fibrillation. The symptoms of auricular flutter depend not so much upon the auricular tachycardia as upon the great increase in the ventricular rate. Auricular flutter may be present in a heart that is apparently healthy, yet that heart, if the paroxysm be of sufficient duration, will eventually suffer from the great work put upon it and dilatation and venous stasis are not rare sequelæ. There will be a quick return to normal in the healthy heart with the resumption of the normal rhythm. It is, however, quite different with the diseased heart; one with mitral stenosis, for instance; this is a heart which has, perhaps, already lost a great deal if not all of its reserve and it cannot support the burden that has been put upon it and heart failure may result. There are three things which we

may hope to do in these cases, with digitalis, when given in large doses; we may either bring on auricular fibrillation which is temporary and which is followed by a normal rhythm, or the fibrillations may remain permanent, or we may be forced to give digitalis for a long time and not succeed in more than reducing to within normal limits the ventricular rate. Those cases in which fibrillation remains permanent certainly are improved subjectively; they lose that sensation of oppression in the chest and that feeling of fluttering in the region of the heart. In those cases in which we only succeed in increasing the heart block we can prolong the life of the patient for many years.

The case which Dr. Oertel has shown is particularly interesting in association with the last slide Dr. Meakins presented. I remember a case of complete heart-block under Dr. Finley, with Stokes-Adams syndrome extending over a year. With each fit for three minutes there would be no heart sound and no pulse, then the heart would start to beat and then a high-tension pulse of 120. Each time following a fit it would be 120 and gradually within five minutes would slow down again to its normal rate of 32. The slide which Dr. Meakins showed, giving a series of ventricular premature contractions almost presenting tachycardia, was most interesting. My case showed a similar electric curve, a complete heart block, the same dissociation of the auricles and ventricles, and these ventricular premature contractions occurring in succession were the cause of the increase in the pulse rate. The patient died and post mortem examination revealed a large heart with considerable myocardial degeneration. The heart was lost and section could not be made.

PAPER: The use of salvarsan in pernicious anæmia, by Dr. H. A. Lafleur.

DISCUSSION: Dr. C. F. Martin: We are all much indebted to Dr. Lafleur for his very lucid description of the cases he has treated by this method and we are all struck by the fair proportion of cases that have been improved by it. The experience of a good many has been not quite so satisfactory. It seems to me, as I noted the blood count, that none, or comparatively few, if any, have a very high blood count even when most successfully treated; the hæmoglobin rarely rose above 50 per cent. and comparatively few of the red cells rose above three million. However, the subjective improvement seems to be so very marked in some that Dr. Lafleur is to be congratulated. In a few cases in which we have used it in the Royal Victoria Hospital we were not so fortunate in our results. In one

case there was a slight increase in temperature and rigours and the patient went from bad to worse and succumbed to the disease under the clinical picture of septicæmia. A great deal of improvement has followed this treatment, probably more than by any other, and yet I think cases sometimes have improved quite as remarkably by other means; such, for example, as saline injection, transfusion, and sometimes even by the much despised cacodylate of sodium. I think there are a great many cases which will naturally get well for a time no matter what the treatment and although these cases may not be classed as cured they certainly show a very marked improvement.

Dr. M. Lautermann: As one who has had occasion to use a great deal of salvarsan during the past five years, Dr. Lafleur's contribution to-night presents many points of interest to me. It is gratifying to know that the sphere of usefulness for this arsenical preparation is extending. I should like to ask Dr. Lafleur if a Wassermann reaction was made in each one of his cases to exclude lues; some writers have held that pernicious anæmia is often due to latent or remote lues and I have felt myself that it probably might be well to be sure on this point in the treatment of the condition. Another factor that occurred to me, particularly in the second case where the neo-salvarsan had been used, while in the other eleven cases the old salvarsan proper was employed; it occurred to me that neo-salvarsan, being less toxic might possibly have been better tolerated. I have treated three cases of pernicious anæmia with neo-salvarsan, one case of my own and two brought to me by a confrère. The first is still alive and after four years is very comfortable, and one may be justified in regarding this as being cured; the other two cases were both improved, one treated ten months ago is still doing fairly well and still taking arsenic by mouth, the other was lost sight of. I do not know that we can claim for salvarsan or neo-salvarsan, any more than for arsenic, that it will bring about a cure, but there is one thing we can claim for it and that is much more rapid action than any other preparations with which we are familiar, and it does not appear to lose its efficiency when used in relapses, which frequently occur.

Dr. H. A. Lafleur: Of course I sedulously avoided using the word "cured" in this connexion. All I wanted to maintain is that having treated cases of pernicious anæmia for some time, and using various things, I have never seen results quite so good as this. I have treated cases with Fowler's solution and, to begin with, the majority of people do not stand large doses. I hope Dr. Martin

understood that I was not speaking of cure in these cases and I specially laid stress on the fact that I was not by any means going entirely by the blood picture. On the contrary many patients feel very well with a lower blood picture than those with a high one, and they must be really in as good condition. After all, subjective sensations must count for something, and one's capacity for living a more or less normal life. I am just really experimenting with salvarsan and I am quite pleased with it so far; and I have not had other results that are at all comparable to these. As to the Wassermann reaction I think I stated that in some of the reports it was positive and in others negative, but whether the test was done in all the cases I cannot say. As far as neo-salvarsan is concerned, I only used it in case No. 2, and one would expect that this was quite as efficient as the other preparations.

CASE REPORTS: 1. Two cases of diaphragmatic hernia, Dr. J. Stowers.

2. Case of relapsing fever in a laboratory boy who contracted the disease by allowing a tick, which had been brought here from South Africa, to bite him. Dr. J. Stowers.

THE tenth regular meeting of the Society was held Friday evening February 19th, 1915, in the Montreal General Hospital. The members of the Society were the guests of the Medical Board of the Hospital and the following programme was arranged by a committee appointed by the board, of which Dr. E. M. von Eberts was chairman.

PART I (Surgical Theatre): A case of enlarged spleen in a young child; regarded as an early stage of Gaucher's disease, Dr. Blackader. The differential diagnosis between tic and chorea, Dr. Shirres. A diphtheria carrier, Dr. A. H. Gordon. Subacute bacterial endocarditis, Dr. Lafleur. The new department of remedial gymnastics, Dr. Harvey. B. typhosus osteomyelitis, Dr. Hutchison. Nail extension for fracture of femur, Dr. Elder. Case of appendicular gastralgia, Dr. Bazin. Case—Carcinoma of ampulla of Vater; excision; recovery, Dr. von Eberts. Acute hæmatogenous nephritis, Dr. Patch. Decompression for fracture of skull, Dr. Henry; *X*-rays of stomach following gastro-enterostomy, Dr. Wilkins. Vincent's angina, Dr. Hamilton. Fracture of nose; *x*-ray, Dr. Craig.

PART II (Governors' Hall) Exhibits: Typhoid and paratyphoid fever charts, Dr. Lafleur. *X*-ray plates, Dr. Wilkins. Pathological specimens, gross and microscopical, Dr. Rhea. Photo-

graphs of skin diseases, Dr. G. G. Campbell. Apparatus for intravenous anæsthesia, Dr. Hepburn.

Demonstrations: Pathological specimen, Epidermoid carcinoma hand, Dr. Bazin. Laryngeal tumour, Dr. Hamilton. Laryngeal tumour, Dr. Craig. Case—Bone graft for the relief of Talipes equino varus, Dr. Nutter.

PART III (Eye Section): Demonstration in small surgical room of a series of living cases, chiefly congenital abnormalities, Dr. Mathewson.

PART IV: Demonstration of the electro-cardiograph.

Dr. W. Grant Stewart called the meeting to order and Dr. J. Alex Hutchinson was chairman for the evening.

At the conclusion of the programme, coffee and sandwiches were served in the Governors' Hall.

THE eleventh regular meeting of the Society was held Friday March 5th, 1915, Dr. W. F. Hamilton, president, in the chair.

Dr. A. D. Blackader presented before the Society some notes he had made of the New British Pharmacopœia.

CASE REPORTS: 1. Primary syphilis of the conjuctiva. 2. Fibroma of the orbit, by Dr. G. H. Mathewson.

Dr. L. J. Rhea showed a slide from the fibroma case.

PAPERS: 1. Some observations on eclampsia, by Dr. T. F. Cotton. This paper was discussed by Dr. Horst Oertel and Dr. H. M. Little.

2. Back ache, corsets, and high heels, by Dr. J. Appleton Nutter, illustrated by charts.

THE twelfth regular meeting of the society was held Friday, March 19th, 1915, the president, Dr. W. F. Hamilton, in the chair.

PATHOLOGICAL SPECIMENS: Series by Dr. Horst Oertel

1. *Unusual aortic and pulmonary ulcerative endocarditis with double perforation.* This specimen is from a patient who was in the Royal Victoria Hospital, under the care of Dr. Hamilton and particularly studied by Dr. M. E. Abbott, with a clinical diagnosis of malignant endocarditis. The case will be reported in detail later by Dr. Abbott. Suspicion was entertained during life of the patient that a communication existed between the right and left heart. At autopsy was found an ulcerative and productive endocarditis, extraordinary in position and extent. It involved the pulmonary and aortic valves with their adjoining endocardium. The endocarditis was ulcerative in so far as it had led to great de-

struction of both valves; productive, as it had caused the formation of multiple large polypoid vegetations on the valvular cusps which, by continuity and contiguity had extended to the parietal endocardium on both sides. This is more pronounced on the right side. The vegetations are at least partly organized and are firmly attached to the valves and parietal endocardium. The interest in this case is heightened by the fact that there are two communications between the right and left sides; one from the sinus of Valsalva of the middle cusp of the aortic valve by an aneurismal pouch which is directed towards, and has perforated into, the right ventricle immediately below the pulmonary valve; the second communication is established through the musculature of the interventricular septum immediately below and between septal and middle cusps of the aortic valve by an irregular ulcerated canal. In this regard it is interesting and important to enquire into the possibility of previous developmental cardiac anomalies which might have determined the seat and extension of the lesion. For it is known, of course, that cases of malignant endocarditis may, as their point of predeliction, occupy, particularly, septal cardiac defects. Without going into details as to the complicated development of the heart, we may recall here shortly that heart anomalies occur generally as the result of either of two development faults; first, failure in fusion of primary septa; second, irregular and faulty development of septal limbs. The latter occurs especially through certain inhibitory actions which allow parts of an advancing septum to develop more rapidly than others, thereby destroying developmental continuity. This may happen in the interventricular septum, which divides the ventricles and which develops by a dorsal and ventral limb, the former growing, even under normal conditions, more rapidly than the ventral one. Consequently developmental communications occur almost entirely at the point of fusion of septa, or, occasionally, within the course of a septum. But in this heart neither communication between the right and left ventricle is in a situation which may readily be accounted or by such developmental faults. On the contrary, it appears that development of the septa as well as their fusion and the division of aortic trunk into aorta and pulmonary artery have been quite well performed. If this point is against a developmental communication between left and right heart, we possess, in addition, the anatomical evidences of the perforations themselves. The one is a definite aneurismal pouch whose walls and orifices are beset with necrotic vegetations. The other is a ragged irregular canal

with no evidence of a previous definite communication. It is surrounded by thickened endocardium and vegetations. In view of these facts it appears that the weight of evidence points to a purely ulcerative double perforation between the two sides.

2. *Extensive congenital hydrocephalus in a child of seven months.* The patient was under the care of Dr. Archibald. On the death of the child Dr. Archibald immediately injected both carotids with 10 per cent. formalin, with the result that the specimen was found at autopsy, some hours afterwards, in an extremely good state of preservation. It is quite typical in general character. The tremendously dilated lateral ventricles practically control the whole brain area and this dilatation extends well into the anterior and posterior horns. It is interesting to note that the grey matter of the cortex is relatively better preserved than the white matter. Of the occipital lobe, particularly, all that can be seen is a thin covering, made of flattened convolutions of grey matter with no white substance at all. The basal ganglia are nearly entirely lacking and only anteriorly a part of what appears to be the corpus striatum, over which hangs the choroid plexus, exists. The anterior part of the much dilated third ventricle shows the anterior commissure in the form of a thin thread. The duct between the third and forth ventricle is short and wide and there is no obliteration of the spinal canal. This specimen is interesting because it throws some light upon a disputed point in the pathogenesis of congenital hydrocephalus; namely, whether it is due to obstruction or obliteration within the ventricles or ducts of the cerebro-spinal canal. In this case there was certainly no evidence that any such obstruction, either of developmental or inflammatory origin, existed anywhere. It seems also questionable to me whether cases of congenital hydrocephalus can only be attributed, as has frequently been done, to hyper-secretion of cerebro-spinal fluid. It seems at least plausible to assume that, in addition, a lack of development of brain substance is concomitant and possibly precedes it and that the tremendous increase in fluid may at least partly be accounted for by the lack of normal advance in development of brain substance.

3. *Amyloid degeneration of liver, spleen and kidneys following Pott's disease.* Presentation of a typical "sago" spleen; a liver with a rather diffuse amyloid degeneration, which, however, was not massive but only involved extensively the capillaries; and a kidney with amyloid degeneration of the glomeruli, following a case of Pott's disease and hip-joint tuberculosis.

4. *An unusual splenomegaly.* This extraordinary spleen, which will form the subject of a later detailed publication, was an accidental finding in a recent autopsy of a man who had died shortly after an accident. There is practically no history to this case. The only knowledge we have is that he was struck on the perineum and scrotum by an iron bar while at work, which immediately was followed by great pain and marked swelling of the parts. The following day he was admitted to the Royal Victoria Hospital. The findings then were: male of forty-two years, fairly well nourished with markedly swollen scrotum, size of a grape-fruit, deep purple in colour. Right groin also swollen and discolured as far as the anterior superior spine of the ileum. Of his previous history we only know that he had pleurisy on the right side three years ago. His condition continued fairly good, but on the sixth day after admission evidences of an infection were found which were relieved by multiple incisions in the right groin and scrotum and drains inserted. During the following night he had considerable hæmorrhage and developed rapidly the symptoms of a general septicæmia. He died during the evening of the seventh day after admission.

At autopsy the tissues of the scrotum were found œdematous and gangrenous and the adjoining perineum equally so. There existed also a hæmatoma of the abdominal wall extending from the pubis to about 2 cm. below the umbilicus. The heart showed a marked concentric hypertrophy of the left ventricle. The right pleura showed adhesions between the lobes, but was clean over the surface. On the surface of the lower lobe of the left lung there were a few minute tubercles, and near the base there was a larger calcified, slightly contracted, superficial area, but the apex was free. A very unusual condition, however, was found with regard to the spleen. This occupied almost completely the left hyperchondrium and was adherent by dense old fibrous adhesions to all the surrounding organs and structures. Above it was bound firmly to the diaphragm, on the side to the stomach and tail of pancreas and below to the kidney and supra-renals. On removal it was found very markedly enlarged (weight 1225 gm., measurement 12 × 12 × 9 cm.). The surface showed deep scar contractions, dividing it into irregular lobes and giving the organ somewhat the appearance of the lobated liver in syphilitic cirrhosis, while its surface, however, was not irregular, granular or nodular. The organ as a whole was firm and on section it cut firmly, leaving a smooth surface which presents a very characteristic mottled appearance due to diffuse

irregular markings on a pale greyish ground substance. These markings are made up of reddish streaks, dots and blotches. In addition to these there occur, particularly at the periphery, fibrous scars, corresponding largely to the interlobar depressions and extending into the spleen as irregular trabeculae. These traverse the spleen in the form of whitish hyaline bands which occasionally show a yellowish discolouration. They often surround and follow the course of blood vessels within the splenic substance so that their walls are surrounded by thick yellowish white scar tissue. Where these vessels have been cut in longitudinal section, they may be followed in the form of threads or short bands. Occasionally such blood vessels occur within the previously described hæmorrhagic blotches and streaks. It will be seen from this description that we are dealing with an unusual type of splenomegaly and it is not easy to decide what etiological factor may be responsible for it and how to classify it under the existing categories of splenic enlargement. That it is not due to the septic condition, in other words, that it is not an acute splenic hyperplasia, seems quite certain, but it also does not fit in with the chronic types of splenic enlargement which occur in chronic infections or in diseases of the blood. The microscopic examination, which, of course, has not been completed, seems also to exclude the unusual forms of chronic splenomegaly which are grouped under the term of Gaucher's type. There remains the infective granulomata. Whether we have to do with an unusual form of tuberculosis or syphilis or a lesion related to Banti's disease must be left to a future decision, which I hope to make when the case is reported in detail. It is unfortunate that the clinical history of the case is so incomplete and that no knowledge of blood examination during life is available. The case, aside from its scientific importance, is certainly interesting from a clinical stand-point, for it illustrates how frequently diseased conditions may exist in persons considered healthy for all practical purposes and that only an autopsy will give us all the desirable information.

Discussion: Dr. A. D. Blackader: Dr. Oertel, if I understand his remarks aright, regards the existence in chronic hydrocephalus of any obstruction of the ducts at the base of the brain, which permit fluid to escape from the lateral ventricles, as being disproved. Does he thereby exclude inflammatory processes at the base of the brain producing an occlusion of these ducts as a cause of hydrocephalus? I have always considered that chronic hydrocephalus might be due to several quite distinct conditions,

but have always regarded acute or chronic inflammations of the meninges at the base of the brain as a very definite proven cause of some cases of hydrocephalus in infancy.

Dr. H. Oertel: My remarks were made with reference to developmental or congenital hydrocephalus. I think we must, at the beginning, separate cases of hydrocephalus into two categories, namely, those which are truly developmental and those which are acquired. A considerable number of cases of hydrocephalus which occur after birth belong to the acquired type, and it is quite possible that these occur as the results of inflammatory lesions or obstructions within the ventricles or intercommunicating ducts or meninges. These lesions, however, are, as the case which I presented to-night illustrates, absent in the true developmental hydrocephalus and it, in my opinion, depends upon an inhibition in the formation of brain substance which allows the accumulation of fluid, more or less, as a compensatory process.

Demonstration: A series of fractures, illustrated by *x*-rays, By Dr. F. R. England.

Case Report: Coma with acidosis, in a case of acute artnritis, by Dr. W. F. Hamilton. The patient was a young woman who had just weaned her child and the breasts were still full and active. She developed an acute arthritis and was placed under treatment with sodium salicylate when marked signs of acidosis and coma supervened. The patient recovered. (A full report of this case will appear later.)

Paper: The paper* of the evening was read by Mr. V. H. Mottram of the Physiological Department of McGill University, on Fat metabolism including its relation to acidosis.

Discussion: Dr. A. D. Blackader: The case just cited by Dr. Hamilton is one of much interest. The dose of the salicylate was not in my opinion excessive, and any tendency to the production of acidosis was well safeguarded by the amount of sodium bicarbonate combined with it. The results produced, if they were entirely due to the salicylate, were certainly very rapid in appearing and I think must be regarded as an unusual idiosyncrasy on the part of the patient. Occasionally very marked cases of idiosyncrasy to the action of this drug are reported. I would like to ask Dr. Mottram to tell us the reason of the enlargement of the liver which frequently occurs in acidosis in infancy. In my experience an amount of fat in the infant's dietary exceeding 4 per cent. is very liable to give rise to symptoms of acidosis with marked en-

*See page 603.

largement of the liver. In these cases we meet with vomiting, a peculiar rapidity of breathing, an absolute inability to take food, especially if it contain fat, and a liver, of which the lower margin may reach the level of the umbilicus. In one fatal case in which I was able to secure an autopsy Dr. McCrae stated the liver to be loaded with fat. One of the early symptoms of the development of acidosis is the ammoniacal smell which the urine in this condition develops, owing to the conversion of a portion of the urea in the system into ammonia which is then used for neutralizing the acid in the system, and is promptly eliminated in the urine. I would be glad to be informed by Mr. Mottram whether in the infant we should always regard an ammoniacal odour to the urine as an indication of an early stage of acidosis.

Dr. D. J. Evans: I have been much interested in this paper by Mr. Mottram and also in Dr. Hamilton's case; there is much that is suggestive in both of them. As to the question of the lactation in Dr. Hamilton's case; it has occurred to me that it is possible the symptoms had something to do with it. The breasts were engorged at the time of admission to the hospital and the patient may have been one of those women who are exceptionally good nurses. The urine showed that there was an absorption of lactose; may there not also have been an undue absorption of fat in the same way? If she had not been in a state of active lactation at the time, when the fat metabolism was undergoing active work, there might not have been the same results.

Dr. Mottram's paper as to the condition in pregnancy and during lactation of the fat metabolism is extremely interesting. It has always been an extraordinary thing to me to notice the great similarity in the phenomena of the acidosis of pregnancy, with what one meets in childhood; the symptoms are so similar. I have never understood how it is that women have this acid indigestion in pregnancy. The excessive demands upon the liver in this direction are probably the explanation of this form of acidosis in pregnancy that is so frequently met with. It is probably along this line where the liver breaks down under the strain, that we have the eclamptic state developing, when the condition passes over from the physiological to the pathological. The whole subject is one of great interest. These are the first steps that are being taken up just now by various observers along the lines of the metabolism of pregnancy, and in this study we find the liver and the metabolism of fat playing a very interesting rôle.

Dr. H. Oertel: I think that, in a general way, pathological

anatomists and physiologists are in agreement to-day on the subject of fatty infiltration and we all agree that even an appreciable amount of fatty infiltration may occur in an organ under perfectly normal conditions. On the other hand, I do not believe that all fatty infiltration of organs may be regarded as normal or comes within physiological limits. It is, of course, true that fatty infiltration in itself does not, strictly speaking, constitute a pathological condition of cells, but I think we must admit that excessive and permanent fatty infiltration of an organ marks more or less definitely an injury to its cells and, therefore, makes that organ pathological; for it certainly indicates that the healthy metabolism and the regenerative ability of the organ have suffered and that it keeps itself alive under difficulties with the aid of fat as an easily combustible substance. Thus we see degenerative changes, atrophy, or other nutritive disturbances in cells frequently associated with fatty infiltration, and this may be followed by return to healthy conditions or, in lasting injury, to progressive and permanent fatty infiltration. In these cases fat can be seen to infiltrate gradually the cells of the organ in the form of typical, usually large, fat drops which are deposited within the cell body, where they acquire more and more room at the expense of the protoplasm and gradually squeeze the nucleus towards the cell membrane. Now I think we must, even to-day, differentiate, as much as Virchow did formerly, this form of fatty change in organs from another which Virchow named fatty degeneration, although we hold to-day different views as to its character than he did. This type of fatty appearance in organs occurs usually in more rapid and virulent protoplasmic destructions. It does not, at least in the beginning, show the gradual large fat drop infiltration as previously outlined, but fat or physically fat similar, small, almost pin or dust-like, droplets appear diffusely, although rather irregularly, within cells whose protoplasm and nuclei show the severe qualitative changes incident to rapid disorganization of cell constituents. We interpret this lesion at present as an active cell destruction in which lipoid and cholesterin drops are released from the emulsified non-visible state within normal protopasm. It is this type of fatty change in organs which occurs within severe toxic, often rapidly fatal, lesions and which in its character and genesis seems to stand out more or less sharply from that of fat infiltration by ordinary glycerine esters. Undoubtedly both forms of fatty changes are frequently found combined, probably always in cases where death does not rapidly supervene and when restitution

to integrity takes place, or is at least attempted, in the manner which has been so well described by Mr. Mottram to-night.

Mr. V. H. Mottram: In answer to Dr. Oertel I may say that I do not think my point was that fat infiltration of *any* organ is physiological, but that fat infiltration of the liver is physiological. In no case that I have dealt with can the tissue be called in any way pathological. Histological preparations have always been made and there is no sign of damage to the nucleus, etc. I think I would go so far as to say that fat percentage in the fresh liver may vary between 2 and 22 without there being anything wrong with the liver; but as regards the heart and kidney it cannot go above 3 per cent. without there being something decidedly wrong. We have yet to settle how far a liver can function normally when there is a large amount of fat present. To judge from the literature of the subject you can have big infiltrations without serious consequences.

As regards the case which Dr. Hamilton reported I may say that I have found nothing in a recent view of the action of salicylates to lead one to expect an acetonuria. But there is undoubtedly disturbed fat metabolism in his case and the acetonuria may be not only an indication of the mobilization of fat from the mammary gland but also from the fat depôts. The temperature chart shows that the temperature of the patient went, on February 3rd, below normal and that the acetonuria then developed. I found that my animals at the end of the first day of hunger had a subnormal temperature; they then called on their reserve fat, and after that the temperature went above normal. I would like to suggest that the fall in temperature is the signal for fat mobilization, and that, in Dr. Hamilton's patient there was mobilization occurring on account of the subnormal temperature.

Regarding the point that Dr. Blackader raised, the enlargement of the liver that is seen sometimes in children, accompanied with acidosis, this may possibly be the result of a fatty infiltration. Certainly in a large number of animals I have seen, when there has been an excessive amount of fat in the liver, the liver looks yellow and swollen, feels firm, and tears in a quite different way from that of glycogenic liver.

As regards the ammonia in urine in fat metabolism and acidosis I think it is pretty clear that wherever there is an acidosis you get an excess of ammonia. The two run parallel. The explanation that physiologists give is that it is not ammonia formed *ad hoc*, but ammonia caught on its way to conversion to urea. It is linked with the acid and excreted as such.

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